Archives of Dermatology and Syphilology

VOLUME 2 OCTOBER, 1920 NUMBER 4

A CONTRIBUTION TO THE STUDY OF THE ETIOLOGY OF XANTHOMA MULTIPLEX*

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Until recent times speculation as to the origin of xanthoma multiplex concerned itself chiefly with clinical observations of its association with jaundice, hepatic disease and diabetes. Little distinction was drawn between the several clinical types.

LITERATURE ON THE SUBJECT

Thus, Kaposi, in his treatise on skin diseases, stated "Nothing definite is known concerning the causation of this remarkable affection. It has been attributed to hepatic affections because jaundice has been observed in more than half the cases. But it seems probable that the same process of nodular development may attack the liver and thus give rise to jaundice."

Hyde in his textbook on skin diseases, 1900, said: "There is a growing belief that xanthoma is due to embryonic and local causes."

During the past twenty years much study of the histopathology of xanthoma lesions has been made, and at present there is a fair degree of unanimity concerning their histologic peculiarities. These investigations, however, have dealt almost exclusively with the cellular architecture of xanthoma. There have been even remarkably few theoretical views about the affection beyond the discussion of peculiar cutaneous tumors.

Consideration of the pathology of zanthoma lesions has resolved principally about the question of a tumor of local origin or one due to secondary inflammatory irritation.

Virchow thought that the process is a connective tissue neoplasm accompanied by a deposit of fat or by fatty degeneration. Touton and

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*Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

*Rosenbloom, J.: The Cholesterol and Cholesterol-Ester Content of the Blood in Xanthoma Tuberosum Multiplex, Arch. Int. Med. **12**:395, 1913. Method of Windhaus.

Kobner thought that it is an endothelioma; while Hallopeau and Ehrmann deduced xanthoma to be of embryonic origin analogous to the nevi.

Various observers are now quite well agreed concerning essential facts, but there is divergence of opinion as to whether the process is primarily an inflammatory one or a local tumor of probable embryonic origin.

Pollitzer,[1] who has made a thorough study of the histopathology of xanthoma, classifies xanthoma multiplex and xanthoma palpebrarum as two separate conditions. The peculiarities of the former he ascribes to fatty degeneration of the orbicularis muscle, while the latter variety he regards as a secondary connective tissue hyperplasia.

Pinkus and Pick,[2] in 1908, made studies of xanthoma palpebrarum, xanthoma tuberosum and xanthoma diabeticorum. They found each of these types were composed of the same cellular elements, and they considered them to be "microchemically and microphysically identical." They concluded that the peculiar substance of xanthoma is not fat but a cholesterol-ester, a material supposed to be found in the blood in icterus and diabetes in increased amounts, and that its deposition in the tissues produces the formation of xanthoma.

Pringsheim,[3] in the same year, examined xanthoma tissue of the skin and found certain acetone-soluble crystals present which gave all the reactions peculiar to cholesterol. He believed this substance to be the same as that described by Pinkus and Pick and he thought that the substance (cholesterol) is deposited in xanthoma lesions from the blood.

Chauffard and Laroche,[4] in 1913, claimed that xanthoma is probably caused by an increase of the cholesterol content of the blood serum. He inferred that it is a sign of lipolytic insufficiency of the pancreas and is to be regarded less as a tumor than as a local reaction of the skin to cholesterol present in the blood.

Pollitzer and Wile, in 1912, described infiltration of the perivascular and intercellular lymph spaces in xanthoma lesions with a fatty substance which is present also in newly formed cells. Xanthoma giant cells—on staining with osmic acid—were found to be entirely filled with this substance. These observers reasoned that xanthoma tuberosum represents "an irritative connective tissue hyperplasia in which the extravasation of cholesterol fatty-acid-ester, present in excess in the blood, serves as the stimulus. These observers also stated that

1. Pollitzer: New York M. J. **2**:73, 1899.
2. Pinkus and Pick: Deutsch. med. Wchnschr. **34**:1246, 1908.
3. Pringsheim: Deutsch. med. Wchnschr. **34**:2145, 1908.
4. Chauffard and Laroche: Centralbl. f. Biochem. **13**:102, 1912.
5. Pollitzer and Wile: J. Cutan. Dis. **30**:235, 1912.

Fig. 1.—Xanthoma multiplex lesions on eyelids.

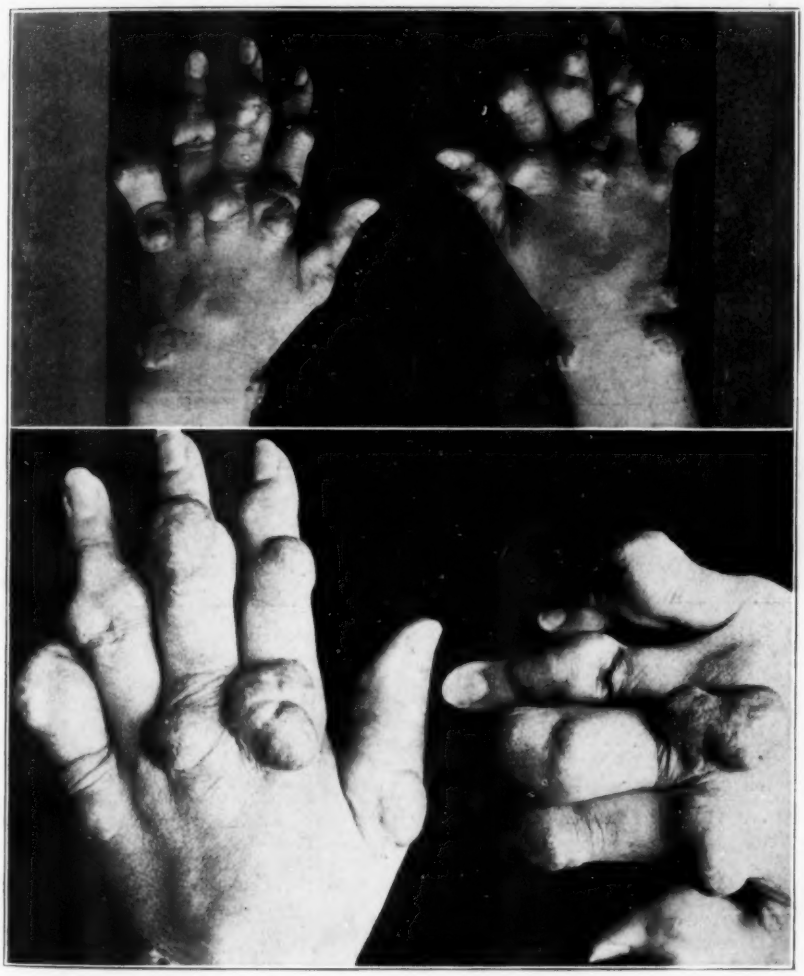

Fig. 2.—Tubercles of hands.

"it is this particular lipoid which it has been demonstrated constitutes the greater portion of the fatty substance in the cells of xanthoma tuberosum."

As it is not definitely stated by Pollitzer and Wile that examination for cholesterol was made from tissue in their case, one may be a little in doubt as to whether their inferences were based on previously reported cholesterol findings, supported by their histologic studies.

Review of the literature respecting the present opinion on the origin of xanthoma multiplex, therefore, shows existing differences. The views held are based mainly on the pathologic examination of skin tissue. Detection of cholesterol as the lipoid material present

Fig. 3.—Gouty lesions of phalanges; blood uric acid increased.

in the tumors from several cases of xanthoma has led to renewed interest in the subject with advancement of the theory that the cholesterol present in xanthoma lesions is deposited there from the blood in which it exists in excess.

So far as I have been able to discover, Rosenbloom,[6] in 1913, is the only investigator who has reported the results of examination of the cholesterol content of the blood in a case of xanthoma multiplex. Rosenbloom examined blood for cholesterol from a patient in the clinic of Dr. George H. Fox. He concluded "that in the case studied there was no increase in the amount of cholesterol in the corpuscles and plasma when compared with a normal control."

6. Rosenbloom: Arch. Int. Med. **2**:395, 1913.

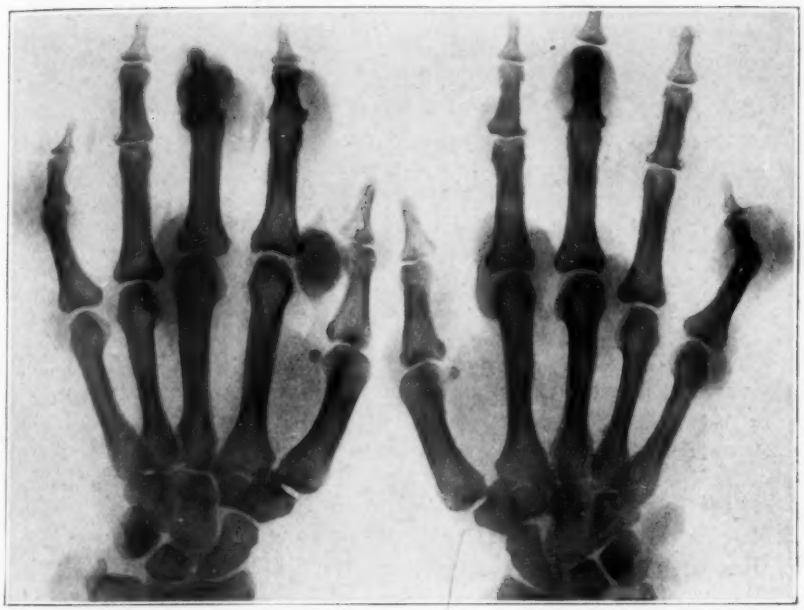

Fig. 4.—Gouty lesions of phalanges; blood uric acid increased.

Fig. 5.—Lesions at elbows.

My purpose is to report the results of an examination of the cholesterol content in the tissue and blood from a case of xanthoma multiplex and to refer to the interesting features of a prominent example of this rare dermatosis.

REPORT OF CASE

Family History.—The patient was a woman, aged 27 years; single, a housekeeper, born in Canada of French Canadian parents. She was a resident of Massachusetts. There was no antecedent history of xanthoma in the family except in one brother who developed the affection at 10 years of age. He had the disease until he was 21 years old, when he died as the result of an accident. There was no history of jaundice, diabetes, cancer, or tuberculosis in the family.

Past History.—The patient was said to have rheumatic fever at 12 years of age. Since childhood she had had occasional attacks of indigestion accompanied

Fig. 6.—Lesions on elbow.

by headache. She had no remembrance of having had jaundice. An attack of diphtheria occurred at 7 years of age.

Present Illness.—The patient's mother told her that the present affection began soon after the attack of diphtheria when 7 years old. Lesions appeared first over the knees and extensor surfaces of the phalangeal joints. The initial lesions grew larger and from time to time new ones appeared over various parts of the body and limbs. After a period of twenty years they attained the existing degree of development and distribution.

Skin Lesions.—There was a generalized eruption of tubercles of various sizes over the arms, legs, feet, gluteal region, eyelids and chin. They were quite symmetrically disseminated, predominated on the extensor surfaces and, with the exception of the buttocks, the trunk was practically free from the outbreak. The chief clinical features of the eruption are plane and tuberose elements, the

former predominating where the skin is thick and rich in subcutaneous tissue, such as the gluteal region and the flexor surfaces of the arms and legs; while the latter kind occur usually over the extensor surfaces of joints.

While the skin lesions are all of one general class, namely, the tubercle, they may be described as of five kinds: (1) palpebral lesions, (2) nodules appearing over the joints, firm in consistence and covered by pigmented epidermis, (3) flat

Fig. 7.—Gouty lesions of phalanges; blood uric acid increased.

nodules, of softer consistency and also covered with pigmented epidermis, (4) large plaques of the texture and color of the kinds just mentioned, and (5) hard tumors, occurring over the bones and seemingly attached to them. These are covered by skin of normal color.

1. The nodules on the eyelids were soft, of pinkish yellow color, round or oval in shape, smooth, sharply defined and raised from 1 to 2 mm. above the sur-

rounding surface, answering the textbook description of being like pieces of chamois skin implanted in the skin. They vary in size from 4 by 4 to 4 by 10 mm. There were three on the upper right lid, one on the lower lid and one at each canthus of the right eye. Around the left eye there were two on the upper lid, one on the lower and one at the inner canthus.

2. The nodules around the joints were distinctly elevated, moderately firm in consistency, salmon red in hue, freely movable and had a tendency to be lobulated. The epidermis was movable over the underlying tumors. On the hands their arrangement showed decided symmetry on the extensor surfaces at all the articulations between the first and second phalanges and at the metacarpophalangeal joints of the index and middle fingers. At the elbows the nodules

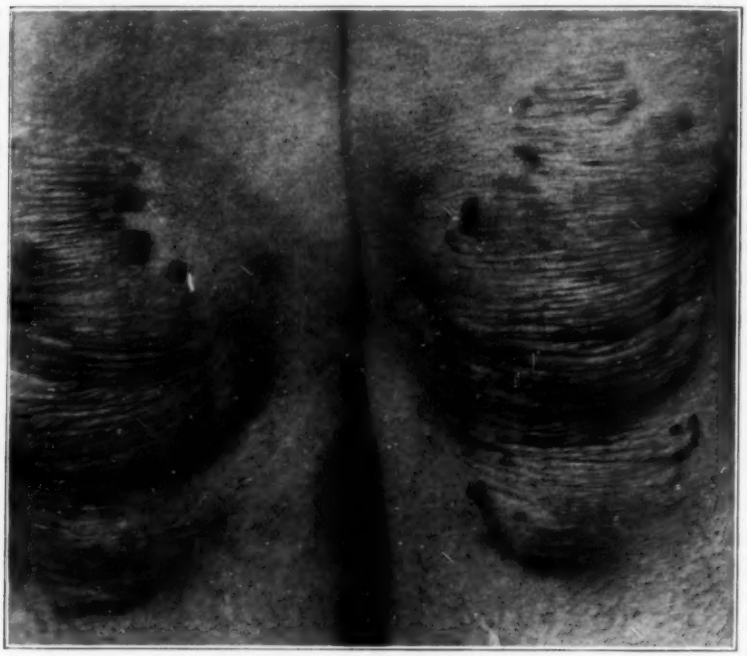

Fig. 8.—Lesions on knees.

were large, hard and freely movable and on the elbow two were attached by a small pedicle of loose skin. On the feet the lesions occurred on the medial surfaces of the great toes, over the articulations of the three outer toes and on the metatarsal joint of the fifth toe.

3. The plane nodules were in general rounded, salmon pink in hue, soft in texture, elevated from 2 to 4 mm., somewhat irregular in outline and roughened on the surface. The borders were sharply defined. They varied from 1 to 4 cm. in diameter. The centers were often depressed. Coalescence frequently took place to form plaques 5 by 12 cm. in diameter.

4. Except for size the plaques were like the lesions just described. They attained their largest size over the buttocks, where they measured 12 by 18 cm. Plaques also occurred over the elbows, the knees and in the popliteal spaces.

Fig. 9.—Nodules on foot and ankle.

Fig. 10.—Lesions on buttocks.

5. The very hard masses appeared at first like exostosis. They varied in size from 1 by 2 to 3 by 2 cm. and were elevated from 0.5 to 1 cm. above the surface of the bone. In most instances they felt osseous, but in some areas they could be slightly depressed and moved a little. Those over the external malleoli were the hardest and the most difficult to move. Elements of this sort appeared on the backs of the hands, over the anterior surfaces of the tibiae and especially around the ankles where they produced marked deformity. Here they were present, not only over the bony surfaces, but also among the tendons of the leg. On the backs of the hands they moved definitely with the tendons.

Roentgen-ray examination subsequently proved the hard tumors to be of soft tissue and presumably similar in character to the others. Attempts to remove

Fig. 11.—Lesions on buttocks.

some of the finger nodules by excision also verified the clinical impression that the xanthoma had invaded the tendon sheaths. In fact, the tendons were so much infiltrated by xanthoma tissue that satisfactory correction of the finger deformity by dissection was quite impossible.

Physical Examination.—The patient was well developed and nourished. General examination was negative except for the cardiac condition. After much examination and discussion, the heart symptoms may be summarized by quoting the opinion of the consulting physician: "She presents the signs of endocarditis of the mitral and aortic valves. These signs are not entirely typical, e. g., the basal systolic murmur with its transmission especially to the right carotid and

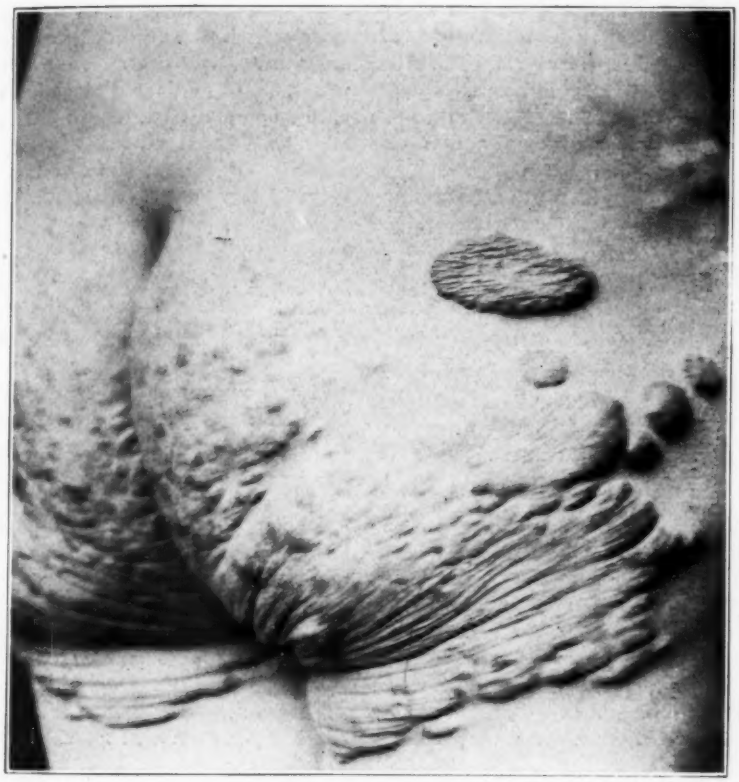

Fig. 12.—Lesions on buttocks.

Fig. 13.—Lesions on buttocks.

also the pulsation in the suprasternal notch. Ordinarily such signs would satisfy one, in an adult, as to the presence of endocarditis with chronic deformity of the aortic and mitral valves. There is nothing in the heart examination that is not consistent with xanthomatous deposits in the endocardium and perhaps in the aorta and great vessels. But, of course, this opinion is entirely inferential."

The Wassermann examination was negative. Urine examinations were repeatedly negative; especially as to acetone and bile. The blood count was normal. The blood uric acid was increased (4.3 mg. per 100 c.c.); the blood sugar was 0.091 per cent.

Roentgen-Ray Examination.—This proved the hard masses over the shins and malleoli to be of soft, probably xanthomatous tissue. The roentgen-ray plates also showed gouty lesions of the hands and feet.

Pathologic Examination.—Several of the large and small lesions were excised for histologic and chemical examination.

Histologic Examination: Examination of numerous sections demonstrated the tissue to be a tumor composed of fibroblasts forming a loose network within which were large vacuolated cells containing apparently a fatty material. There were many needle-like spaces between the fibrils which probably contained cholesterin crystals. About these spaces were small clusters of foreign body giant cells. Sections stained with osmic acid showed the presence of fat in the vacuolated cells and in the lymph spaces.

Chemical Examination of Tissue for Cholesterol: Cholesterol was found in large quantities in three of the nodules examined. Unfortunately the quantitative analysis for cholesterol in tissue was not completed at the time of writing, but this estimation, together with further chemical studies on the case, it is planned to report in a subsequent paper.

Examination of Blood for Cholesterol: Blood was obtained from the patient by the usual method for Wassermann tests. In the examination for cholesterol, as well as for fat in the blood, the method of Bloor[7] was employed; the normal variations for which have been standardized by several hundred examinations of normal blood.

Blood was examined under three regimens of diet. Two analyses were made under usual mixed diet, one after a week on low fat diet, and one following a week under high fat diet. In each case the fasting blood (fourteen hours after food) was used. In order to exclude the possibility of acidosis affecting the cholesterol findings, the urine was examined repeatedly for acetone by the delicate Scott-Wilson reagent. At no time did the patient display any clinical symptoms of acidosis.

The wide variation in the quantitative figures between Rosenbloom's results and those in my case are apparent and even startling. Those of Rosenbloom fall below the normal limits as established by Bloor, whose method for the estimation of blood cholesterol and blood fat is the one now accepted and used in the department of biologic chemistry of the Massachusetts General Hospital.

Explanation of these differences has been sought, but the only interpretation of them to be offered lies in the greater delicacy of recent methods used for cholesterol estimation. I am informed by

7. Bloor: J. Biol. Chem. **24**:223, 1916; idem. **27**:377, 1914.

Dr. Willey Dennis, chemist at the Massachusetts General Hospital, who has carefully verified all the quantitative estimations given in this paper, that the greater accuracy of procedures for the detection of cholesterol used during the past five years warrants the assumption that quantivation by the method employed is the more accurate.

TABLE 1.—XANTHOMA MULTIPLEX: CHOLESTEROL CONTENT IN BLOOD

		Cholesterol	Fat	Alkali Reserve
Jan. 15	Normal diet	660 mg. (0.66%)	2,000 mg. (2%)	
Jan. 18	Normal diet	650 mg. (0.65%)	1,700 mg. (1.7%)	
Jan. 30	Low fat diet	660 mg. (0.66%)	1,400 mg. (1.4%)	
Feb. 7	High fat diet	999 mg. (0.99%)	1,000 mg. (1%)	48.1 volume per cent. normal

Cholesterol content in blood. Fasting blood (14 hours after food).
Normal cholesterol 210 to 240 mg. per 100 c.c. (0.2 per cent.) } Method of
Normal fat 300 to 400 mg. per 100 c.c. (0.3 per cent.) } Bloor

TABLE 2.—CHOLESTEROL CONTENT IN BLOOD*

	Blood Corpuscles	
	Cholesterol	Cholesterol-Ester
Xanthoma tuberosum	65 mg. (0.065%)	Trace
Control	68 mg. (0.068%)	Trace
	Blood Plasma	
	Cholesterol	Cholesterol-Ester
Xanthoma tuberosum	48 mg. (0.048%)	22 mg. (0.022%)
Control	46 mg. (0.046%)	28 mg. (0.028%)
	Total Cholesterol Content in Blood	
Xanthoma tuberosum	135 mg.	
Control	142 mg.	

* Rosenbloom, J.: The Cholesterol and Cholesterol-Ester Content of the Blood in Xanthoma Tuberosum Multiplex, Arch. Int. Med. **12**: 395, 1913. Method of Windhaus.

Cases of xanthoma with cardiac symptoms, subsequently proved at necropsy to be due to xanthoma deposits in the endocardium, have been reported by Lychzen and Knauss, Pavy and Fagge and by Noxon. Cranston Low [8] refers to a case of xanthoma in a girl 11 years old, who showed heart symptoms similar to those in the present case. Low's opinion as to probable existing xanthoma of the heart was necessarily inferential, as is my own.

Other cases of xanthoma with cardiac lesions of unproved etiology have been reported by Poenngen, Pollonon, Vidal and Gynne.

SUMMARY

The cholesterol blood content in this case was found to be considerably increased under normal mixed diet, under low fat diet and under high fat diet. Under high fat diet the increase was excessive. Cholesterol was also found in large quantities in all xanthoma lesions examined.

8. Low: Brit. J. Dermat. **22**: 109, 1910.

From the findings referred to above it seems probable that xanthoma multiplex is a dermatosis whose origin lies in the increased amount of cholesterol in the blood, the skin lesions of which are caused by its deposition in this tissue where it induces a peculiar secondary connective tissue hyperplasia.[9]

In conclusion, I desire to give full credit to Dr. Willey Dennis, chemist at the Massachusetts General Hospital, for making the chemical examination and to acknowledge to her my thanks for verification of all the quantitative figures submitted.

237 Marlborough Street.

DISCUSSION

DR. FORDYCE said he had recently had a case of extensive xanthoma multiplex in which the cholesterol content in the blood was increased. Although the case clinically was similar to xanthoma diabeticorum, the urine was free from sugar.

DR. POLLITZER thought it was gratifying to find in this complete report a corroboration of the findings which he and Dr. Wile had advanced some years ago. Dr. Burns agreed that the lesions were the result of an irritative connective tissue hyperplasia, as the result of the deposit of cholesterol fatty-acid-esters in the tissues. He thought this particular feature might now be regarded as established. At the time they made their studies the methods of the determination of cholesterol in the blood were extremely crude. In regard to the variations which had been found in different reports, it is evident that there must be a variation in the normal cholesterol fatty-acid content in the blood. That there was an increase in these cases seemed established, but it did not follow that the lesions would disappear when the cholesterol fatty-acid-esters in the blood were reduced. They might remain long after the true cholesterolemia had ceased to exist. On the other hand, there was probably a certain amount of absorption going on from the lesions back into the blood. This was apparent from the fact that these lesions were found after many years undergoing a spontaneous reduction in size, and in some instances they had been known to disappear. This must be due to absorption back into the blood, so one might find at one time in a given stage of xanthoma tuberosum an excess in the blood during the active stage of this disease; when the disease was stationary and no new lesions were forming, a normal cholesterol content, and later, if absorption took place, there would again be an increase in the cholesterol content. In the case reported by Dr. Burns the increase was approximately 300 per cent. over the normal of two tenths of 1 per cent. on a regulation diet. In his opinion the case presented a further corroboration of the fact that xanthoma tuberosum was a systemic disease due to excess of the cholesterol fatty-acid-esters in the blood. The lesions tend to form about the joints where there is motion—flexion and extension—and at such points there must be alternations in the local tension on the blood vessels, affording opportunities for the chemical elements dissolved in the blood to be forced out rather than at other points where no such pressure-changes existed.

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9. In addition to the references already given, the following may be of interest:

Knowles: J. Cutan. Dis. **22**:288, 1914.

DR. WILE expressed his appreciation of Dr. Burns' paper and stated that the association of xanthoma tuberosum and diabetes was undoubtedly due not to the presence of sugar, but to the associated cholesterolemia, which was found in the latter disease. Dr. Wile called attention to another form of peculiar yellow pigmentation that occurred in diabetes frequently at the end stage of the disease, to which attention had first been called by Van Noorden. This peculiar color is found on the palms and soles and occasionally on the face. It seemed likely that this color was due to the deposition of cholesterol associated with the diabetes in the fascia and fat of the regions affected.

DR. STOKES thought it might be interesting to recall the work of Anitschkow in which he succeeded in artificially inducing the formation of xanthomas in the rabbit by administering large amounts of cholesterol by mouth and then traumatizing the skin. The xanthomas developed only at the sites of trauma.

DR. HIGHMAN said he was about to quote the article referred to by Dr. Stokes. The author fed lecithin to rabbits in great quantities, but until he traumatized the skin he could not produce the formation of xanthoma lesions. After placing setons in the skin they developed, which made it evident that it is necessary to have some local disturbance in the skin before xanthoma develops. The lesions, after placing the setons, were typical in every detail of those of xanthoma.

DR. POLLITZER said the work of Dr. Hess tended to show that the peculiar yellow color was due to a pigment and not to cholesterol—to a pigment derived from vegetable matter. Diabetic patients are fed largely on green vegetable matter, which contains a large amount of coloring material that has been called carotin from the fact that it is most abundantly found in carrots. It had been found that it was possible to color a baby yellow by feeding it carrots. Dr. Hess had demonstrated this in babies in New York and this discoloration occupied in large part the regions which are called seborrheic, the yellowish tinge appearing notably in the face and in the nasolabial folds. Cessation of the feeding of carotin results in a gradual disappearance of the yellow discoloration, very often with desquamation.

DR. BURNS (closing) said that his paper was presented only as a single observation and he had made no attempt to draw conclusions, since this was probably the first reported case of xanthoma multiplex in which increase of the cholesterin content in the blood was observed.

Dr. Burns thought the observation of the excessive cholesterin content in the blood in cases of xanthoma multiplex ought to be confirmed by further work. In diabetes it was recognized that cholesterol existed in some cases but not in others. The variation in the cholesterol content of the blood in diabetes is enormous, but its relation to the disease is little understood. It may be that xanthoma diabeticorum occurs in the presence of excessive cholesterol, but this view is entirely speculative as little work has been done up to the present time on the relation of xanthoma diabeticorum to this content.

NOTES ON TWO UNUSUAL CASES OF DARIER'S DISEASE

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So many instances of Darier's disease have been recorded in the past thirty years that the mere recital of the symptomatology and description of the histopathologic changes in new cases ceases to be of more than passing interest. All the literature relative to the disease throws not one ray of light on the obscure problem of its etiology; the entire question of causation is as much of an enigma today as it was between 1889 and 1891, when J. C. White, Morrow, Darrier and Thibault published reports of their cases. Referring to its etiology, Jadassohn said that in his opinion the disease belongs in the group of congenital anomalies of cornification, and that it may occur in combination with various anomalies in the same individual, or may occur in the same family. In 1916, Boeck, in demonstrating some patients before the dermatologic congress in Christiania, stated that these individuals are often inferior physically and that they sometimes display evidences of "moral insanity." [1]

Malcolm Morris [2] expressed the opinion that the etiology rests on an endocrine basis, and Strandberg [3] of Stockholm also is strongly in favor of accepting this view, more especially as a working basis for research. The latter directs attention to two points which are at least suggestive: the dystrophic affections of the nails in many of the cases; and the fact that in some instances exacerbations of the eruption have manifested themselves during pregnancy. Macleod [4] published an interesting paper dealing with this subject, calling attention to the fact that Darier himself suggested that this affection was possibly due to a functional insufficiency of the thyroid, but benefit has not so far followed the employment of the remedy in it.

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1. This observation certainly does not accord with my experience. I have seen eight cases, none of which conveyed the impression of being mentally deficient (F. W.).

2. Morris, Malcolm: Internal Secretions in Relation to Dermatology, Brit. M. J. **1**:1037 (May 17) 1913.

3. Strandberg, James: Beitrag zur Frage der Bedeutung der inneren Sekretion in der Dermatologie, Stockholm: Isaac Marcus, 1917.

4. Macleod, J. M. H.: Hormones in Relation to Diseases of the Skin, Practitioner **94**:298 (Feb.) 1915.

Marked advances have, nevertheless, been made in the realm of therapeutics. Radiotherapy can do much toward amelioration of the symptoms; in fact, there is no reason why the judicious employment of roentgen rays should not cure the eruption entirely, with the aid of baths and mild emollient ointments.

The two cases forming the subject of these notes present certain features which we believe of sufficient interest to merit being recorded. Both patients were referred to one of us in private practice.

REPORT OF CASES

CASE 1.—The first was an old man, M. L., whose history was first recorded by Bulkley[5] in 1890 and by Lustgarten and Piffard[6] in 1891. At some period or other of his long career, as a remarkable and striking example of Darier's disease, this patient had graced the offices and clinics of probably all the older dermatologists in this city; and, indeed, he always conveyed the impression of priding himself on the distincton of being the "star case" in the many dermatologic meetings at which he was a subject for demonstration. The first symptoms of the eruption appeared in 1864; he consulted Piffard about 1880 and about ten years later Lustgarten and also Bulkley. One of us (F. W.) saw him in June, 1917, when he was about 75, his disease having existed fifty-three years. At the time of his visit, the eruption was very extensive and the infiltrations in the skin were very pronounced, but the man complained more of annoyance and discomfort than actual itching or sensations of pain. He said that the eruption had changed very little in the preceding twenty years.[7] At the time of this observation, however, a well developed basal cell epithelioma was noted on the right side of the bridge of the nose.

Detailed accounts of this case appear in the papers alluded to and as the lesions had undergone very little change since these papers were published, further description would be superfluous. Piffard's article contains an excellent photomicrograph of sections prepared at the time by Fordyce; the characteristic *corps ronds* are here beautifully illustrated. On looking up the various articles dealing with his case, we were surprised to find that a photographic reproduction of his eruption had been omittted in these publications. This seemed to be all the more remarkable, considering the fact that Lustgarten presented a photograph of the eruption before the tenth international dermatologic congress, which met in Berlin in 1890. The opportunity was therefore taken, at the time of the patient's visit, to obtain a photograph of the eruption as it appeared in 1917. At the same time, a small piece of diseased tissue was removed, to furnish material for further study.

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5. Bulkley, L. Duncan: Psorospermosis Follicularis Cutis, Med. News (Nov. 8) 1890.

6. J. Cutan. & Genito-Urin. Dis. **9**:7, 14, 1891.

7. We were informed by the patient's attending physician, Dr. B. F. Ochs, that he died only recently in New York of pneumonia.

The appended illustrations (Figs. 1, 2, 3 and 4) convey a good idea of the more recent appearances presented by the diseased skin.

A rather interesting feature in connection with the family history is the statement made by Bulkley in 1890 and by Lustgarten in 1891 to the effect that none of the patient's children presented any eruption. Only recently we were informed by Dr. B. F. Ochs that one of the patient's daughters had an eruption of Darier's disease, almost as extensive and severe as that of her father. Disheartened by the unresponsiveness to the many forms of treatment which her father had undergone for so many years, she had steadfastly refused to submit to any attempts at therapy. She died recently, aged about 38, of endocarditis. We were unable to ascertain just when the daughter first exhibited the changes in her skin, but it is evident that her skin was unaffected in childhood, thirty years ago, when Lustgarten presented his paper dealing with her father's malady. This hereditary and familial incidence is, of course, a significant feature of the disease, most of the patients giving a history of the same affection existing in other members of the family.

In striking contrast to the extensive and severe eruption in the foregoing case, our second patient, a young woman, presented what might be termed the opposite extreme: The earliest lesions of the disease, appearing in the form of inconspicuous, widely scattered, rather vaguely defined efflorescences, giving rise to no subjective sensations and constituting nothing more than a cosmetic disturbance. Instead of an eruption which permitted identification at a glance, as in the first case, the lesions in this patient were so far from characteristic that a clinical diagnosis was arrived at only tentatively. Microscopic examination of sections of the lesions was necessary to establish the diagnosis of Darier's disease. An interesting feature in this case was the coexistencce of distinct spots of macular atrophy on the chests and breasts, intermingled with numerous *lineae atrophicae* (vergetures) in the same and in neighboring areas of the skin. The coexistence of Darier's disease and atrophia maculosa cutis has not, so far as we are aware, been recorded before.

According to Darier, "so-called abortive or incomplete cases are not very uncommon." Only recently a case of this kind was described from the Vanderbilt Clinic by Scheer.[8]

Case 2.—Miss J. Z., aged 21, was referred to us March 11, 1920, for consultation. The family and personal histories were entirely negative. No other member of the family, immediate or remote, had, so far as she knew, been afflicted with any skin disease.

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8. Scheer, Max: A Case of Darier's Disease in Its Early Stages, J. Cutan. Dis. **34**:837 (Dec.) 1916.

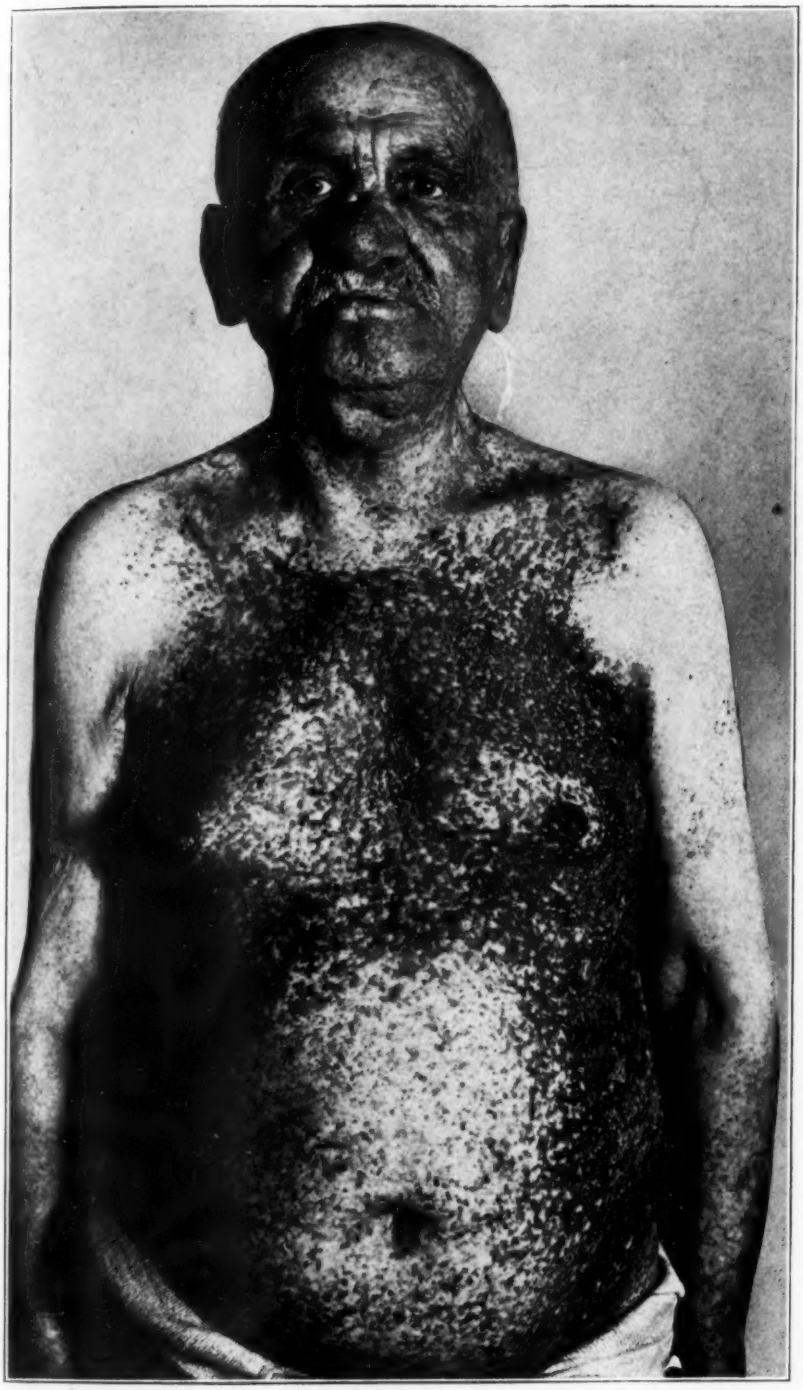

Fig. 1 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the anterior aspect of the body and the site of a basal cell epithelioma at the bridge of the nose.

Physical Examination.—This revealed no other abnormalities than the eruption on the skin, with the exception of obesity, the weight being about 175 pounds; she was of average height for her age. With the object of trying to discover if there might be some obscure disturbance of the glands of internal secretion, the girl was referred for consultation to Dr. Walter Timme, to whom we are greatly indebted for his painstaking examination, directed chiefly toward endo-

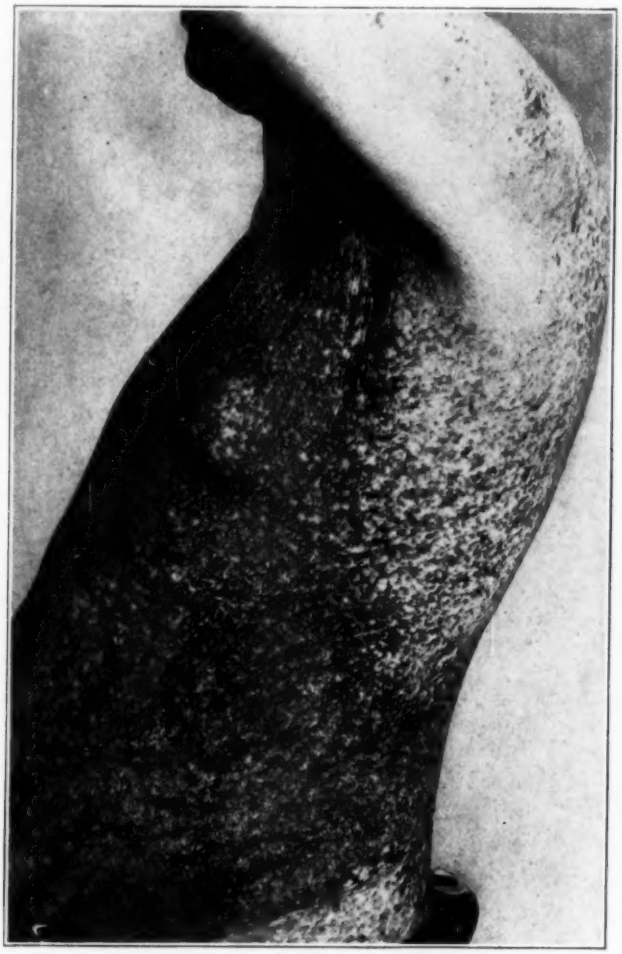

Fig. 2 (Case 1.)—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the lateral aspect of the trunk and arm.

crine changes. Dr. Timme reported negative findings; physical examination, chemical examination of the blood, as well as radiographic examination of the sella turcica failed to reveal the slightest abnormalities. The patient stated that she had always been in good health.

The skin of the patient exhibited two entirely different types of eruption (Figs. 5 and 6). In the axillae, on the back and on various areas of the chest and breasts, there was a variety of efflorescences, nearly all of which were

follicular and more or less elevated and hyperkeratotic; these were the elementary lesions of Darier's disease. On the anterior surfaces of both breasts, from about the level of the nipples to the clavicles, as well as on both sides and the front of the neck, there were many dime-sized, round and oval, faintly scaly, very slightly depressed macular areas, which glistened slightly when viewed in oblique light; intermingled with these, in the same areas, there were numerous pearly-white, somewhat depressed parallel bands running up and

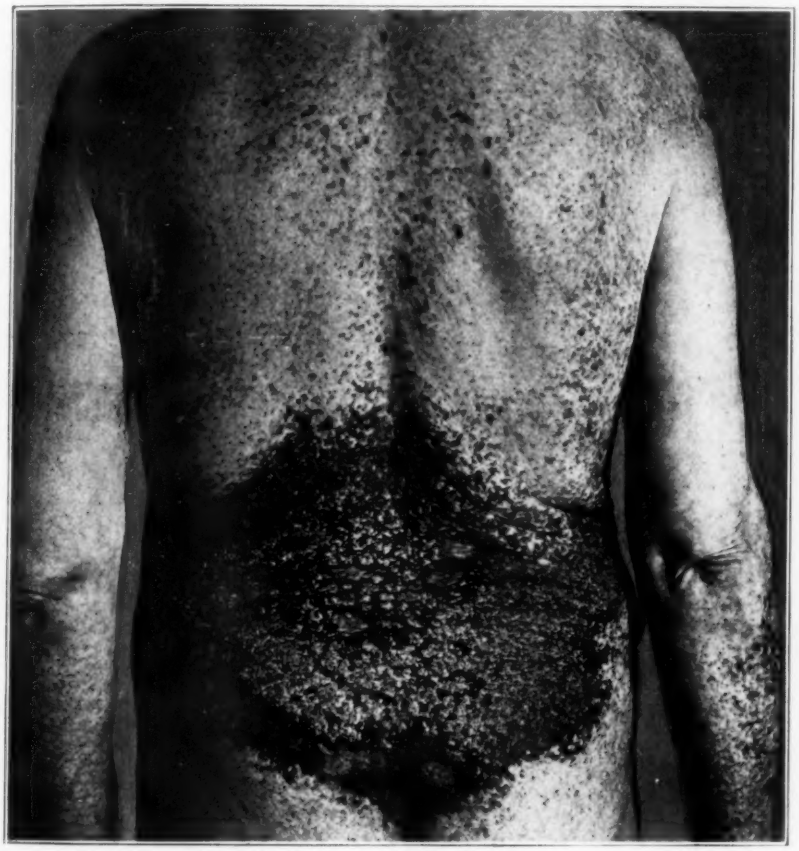

Fig. 3 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the eruption on the posterior aspect of the trunk.

down both breasts and radiating into the armpits and toward the neck and shoulders. These patches and bands were quite typical lesions of atrophia maculosa cutis and lineae atrophicae.

The lesions of Darier's disease were most pronounced in the armpits. Here they formed dark brown rounded patches of closely aggregated, short, filiform, wart-like protuberances, rather soft to the touch and of a shaggy appearance. The axillary hair was sparse. The clinical appearance of these axillary lesions

so closely simulated that of acanthosis nigricans[9] that the differential diagnosis hung in the balance until sections of the skin were examined. The greater part of the mid-portion of the back exhibited many scattered and confluent follicular hyperkeratoses, most of them the size of a pin-head and capped by a tiny scale. In some places the confluence of these follicular lesions produced small patches of irregularly shaped, dark brown, somewhat crusted lesions, the crust being greasy and readily detachable. Similar but less abundant follicular keratotic elements were also present on the anterior surfaces and between the breasts, and a few were scattered over the skin of the abdomen. There were no lesions anywhere below the waist-line, nor on the face, scalp and upper extremities. (The small crust-covered spot on the back, Fig. 6, is a biopsy wound.)

The macular and linear atrophic changes have in part been described; the illustration (Fig. 5) shows the atrophic bands on the breast and the rugose patch of Darier's disease in the armpit. Numerous atrophic striae are seen traversing this patch in various directions.

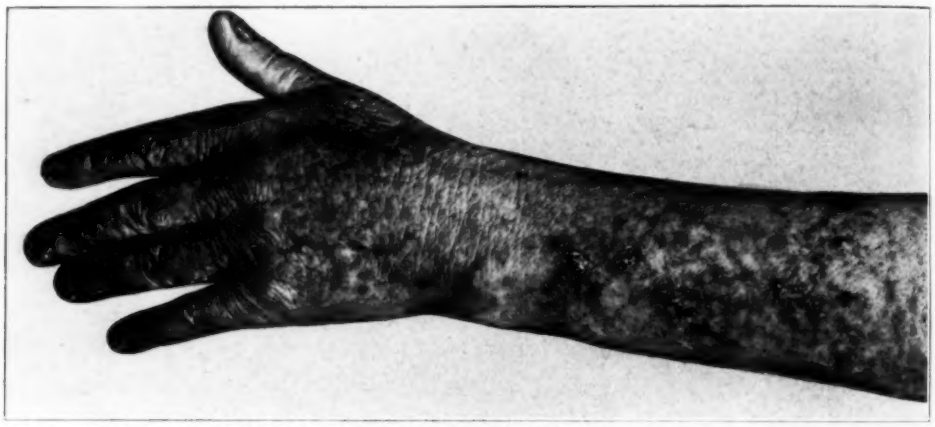

Fig. 4 (Case 1).—Psorospermosis follicularis vegetans (Darier's disease), showing the warty and crusted lesions on the back of the left forearm and hand, and the distrophy of the nails.

The patient first noticed thickening and discoloration of the skin of the armpits about eight years ago, when she was 13 years old. The follicular keratoses of the trunk followed several months after the appearance of the axillary lesions, and slowly increased in number and extent. The atrophic bands and oval lesions were first noticed on the neck and breasts three years ago. The girl had been quite stout since early childhood; there had been no sudden variation in the amount of fat underlying the skin of the neck and chest.

Histopathology.—A small piece of tissue was taken from the armpit for microscopic examination. The section presented a hyperkeratotic epidermis of irregular outline; the papillae were hypertrophied and thrown into folds, the

9. We had the opportunity of comparing the axillary lesions of acanthosis nigricans with these similarly situated patches of Darier's disease, and were unable to tell them apart by the naked eye; even palpation revealed no differences.

rete pegs being long and narrow, and their cells edematous. Parakeratosis was absent. The follicles were distinctly dilated, some of them filled with horny masses. In the corium, the lymph spaces were distinctly dilated; the collagen was edematous. There was moderate edema of the walls of the blood vessels, with a sparse infiltration of small round cells, fibroblasts and a few epithelioid cells.

Although two or three refractile round bodies were demonstrable in various parts of the epidermal layer, the characteristic *corps ronds* or "psorosperms" of Darier's disease could not be positively identified. Another section was therefore removed, this time from the skin of the lumbar region of the back.

Fig. 5 (Case 2).—Psorospermosis follicularis vegetans (Darier's disease), showing the rugose vegetations in the armpit and the striae atrophicae and macular atrophic spots on the breast and in the axilla.

This section consisted of nothing more than a few follicular keratotic papules the size of a pin head, evidently the earliest visible lesion of the disease, clinically indistinguishable from ordinary keratosis pilaris. In this specimen the microscopic changes were practically the same as those just described, excepting that the horny layer was much thicker than that of the first section and the collagenous tissue in the pars papillaris was more edematous and took the stain poorly. The rete contained many vacuolated cells, some of them containing granular

Fig. 6 (Case 2).—Psorospermosis follicularis vegetans (Darier's disease), showing the early follicular keratotic lesions on the back, both isolated and confluent, the latter crusted. The dark crusted lesion to the right of the median line is a biopsy wound.

bodies, others showing deformed and shrunken nuclei; here and there, chiefly in the upper layers of the rete, were seen isolated and grouped round refractile bodies with well defined limiting membranes—the *corps ronds.*[10]

Treatment.—Boric acid ointment was prescribed to anoint the affected regions of the skin, and to retard the formation of scales and crusts. At the same time, roentgen ray treatment was applied to the lesions on the chest, back and in the armpits, in ¼ H. unit doses (skin distance), once in two weeks. After six such treatments, all the lesions of Darier's disease, save those in the axillae, had entirely disappeared, leaving no trace; at the present moment (the patient being still under treatment) the armpit patches show 75 per cent. improvement. The patient was particularly perturbed about the macular and linear atrophic lesions on the chest, neck and upper portions of the breasts, these areas being more or less exposed in the wearing of summer apparel. We informed her that we feared little could be done toward remedying these defects—that they were probably incurable. We were gratified as well as astonished, therefore, to find that both the linear and macular lesions faded away completely in all regions exposed to the roentgen ray, so that today the skin appears to be quite normal in every respect. The patient also received one-tenth grain of thyroid gland extract three times a day. Whether or not this medication had any direct or indirect bearing on the cure of the atrophic lesions, or whether their disappearance may be attributed to the influence of the roentgen rays alone, administered to the follicular keratoses occupying the same fields of the integument, we have as yet been unable to decide. Perhaps the combination of roentgen rays, thyroid extract and massage produced the unexpected result.

To judge from the rapid disappearance of the lesions of Darier's disease on the trunk, it is safe to anticipate a complete restitution to normal conditions, with respect to the remaining keratotic formations in the armpits, after a few additional roentgen ray treatments.

COMMENT

These two examples of Darier's disease are briefly recorded with the realization that, although nothing new is brought out regarding our knowledge of the disease, they at least possess certain features of peculiar interest to the dermatologist, aside from being mere case reports. Viewed from the morphologic standpoint alone, comparison of the two eruptions offers a fascinating clinical study: In the old man it is interesting to note the almost universal integumentary changes, their development and persistence over a period of more than half a century, their recalcitrance to many forms of treatment, and the occurrence of an epithelioma of the face, presumably at the site of one or more follicular keratoses. Compare these to the picture presented by the young woman: an inconspicuous, rather ill-defined eruption of isolated and irregularly grouped follicular keratoses on portions of the chest and back, of eight years' duration, together

10. Drs. Fordyce and Pollitzer, who kindly examined these sections for us, confirmed the microscopic findings.

with more pronounced hyperkeratotic formations in the armpits, the coincidence of macular and linear atrophic lesions of the same fields of skin, and finally, the good results obtained by radiotherapy.

To revert to the question of etiology: In recent years the impression has grown among internists and dermatologists, that the rôle of the ductless gland secretions cannot be ignored in the search for the pathogenesis of certain obscure skin diseases, more especially with regard to certain atrophies, dyskeratoses and anomalies of cornification. Attention has been especially directed toward such affections as ichthyosis, mal de Meleda, Darier's disease, scleroderma, atrophoderma, trophic diseases of the nails, Raynaud's disease, and others. Osler, Malcolm Morris, Macleod, Johnston, Strandberg, Weiss, Foerster, McEwen and many others have contributed to the literature on this phase of dermatotherapy. The therapeutic results have thus far been meager, but, in a few instances, they have been at least sufficiently encouraging to justify the undertaking of careful investigations of possible *endocrine* changes in patients affected with these several ailments, together with the institution of a rational therapy where indicated. He who reads the transactions of dermatologic society meetings will find that discussions concerning the ductless glands and their relation to the pathogenesis of some skin diseases are becoming more and more frequent. It is true that not all of these discussions attain the high standard of logical argument demanded by science; oftentimes they are tinged with facetious, cynical, even acrimonious periods, which, though amusing to the listener, are in no way helpful to those who are groping in the dark in the search for facts. In the field of research work, nothing can be gained by such crude subterfuges. The whole subject of endocrinology in the realm of dermatology is as yet deeply shrouded in a veil of obscurity; every phase of it must be approached with an open and receptive mind, if the wheat of certainty is to be separated from the chaff of conjecture.

The writers are greatly indebted to Dr. Geo. M. MacKee for the photographs, and to the staff of the pathologic department of Prof. Fordyce's clinic for the microscopic sections.

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LUPUS ERYTHEMATOSUS AND FOCAL INFECTION*

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REPORT OF A CASE

Mrs. B., 35 years old, was referred to me in May, 1918, for the treatment of an erythematous lupus of one year's duration. The eruption, while presenting a wholly characteristic appearance, was distributed over an unusually large area; coin-sized and smaller patches were scattered over the cheeks, the upper and lower lids, behind the ears, in the scalp, on the upper chest, the arms and forearms and in the interscapular region. Some of the larger patches, especially those on the malar eminences, the upper lids and the back, were decidedly thicker and more scaly than usual. Before coming under my care a diagnosis of syphilis had been made and antisyphilitic remedies had been employed for some months, of course without influencing the disease. Under the local use of a 2 to 3 per cent. alcoholic solution of salicylic acid and the internal administration of quinin in considerable doses, there was a steady but slow improvement in all the patches; on the back and arms the improvement was especially noticeable, the disease disappearing in these regions in the course of a few months. Other local remedies were tried from time to time, but the salicylic acid seemed by far the most effective. After nearly a year of this treatment, improvement ceased and as there had been no new patches, trichloracetic acid was applied to the thicker lesions at intervals of some weeks, the intervals between the applications being longer than was desirable because of the distance at which the patient lived from Philadelphia. These applications were of undoubted value, but as the patient found them extremely painful they were discontinued and phenol every few days substituted, the patient making the applications herself. Two months later a decided improvement was noted, and the treatment was continued. In the latter part of January of this year a most extraordinary change was observed in the disease—all of the patches were apparently undergoing rapid involution and some of the smaller and less pronounced ones had almost entirely disappeared. It was then learned that this remarkable improvement had followed immediately on the extraction of a "capped" tooth which a roentgen-ray examination had shown to have an abscess at the root, although it had not given the patient any trouble for years. On extraction the roots of the tooth were found to be badly necrosed. Unfortunately, under the circumstances, a bacteriologic examination of the abscess was impossible; this is greatly to be regretted since it leaves us in entire ignorance of the character of the organism concerned in the infection. I had hoped to see this patient again before the completion of this paper, but circumstances have made that impossible. In a recent, letter, however, she states that there has been further improvement.

This case is reported simply for what it is worth—not as proving or disproving anything as to the etiologic relationship of focal infec-

*Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

tion to erythematous lupus, but to put on record a case which is, to say the least, suggestive to a considerable degree of the possibility of such a relationship.

OTHER CASES

A few years ago, Barber [1] reported an extensive case of acute erythematous lupus following the ordinary chronic type after some years, accompanied by high temperature and other grave symptoms threatening, for a time, the patient's life, in which a bacteriologic examination of the feces revealed the presence of large numbers of *Streptococcus longus,* the organism growing in almost pure culture on inoculated mediums. After an illness lasting for a month or more, the patient recovered, the eruption vanishing rapidly. With the improvement in the eruption the streptococcus disappeared from the feces. In Barber's opinion, the disease was due in this instance to the absorption of a toxin produced by the streptococci found in such abundance in the intestinal canal. No mention was made of any local focus of infection and apparently no search was made for it beyond the examination of the feces. Recently [2] the same author has reported two cases of erythematous lupus of the ordinary type associated with an infection of the tonsils by the same organism found in the former acute case; and from a series of similar cases which he has been able to collect recently he is convinced that the disease is due "in some instances at any rate" to the toxins produced by *Streptococcus longus.* In one of the reported cases treated by an autogenous vaccine prepared from the tonsils, an injection of a dose containing 5,000,000 of the organism was followed by a decided reaction in the patches of lupus lasting twenty-four hours; and after a larger dose, one containing 10,000,000, an intense reaction followed, together with considerable constitutional disturbance. The streptococcus in this case was found not only in the tonsils, but also in adenoid tissue at the back of the throat, the patient having suffered from adenoids some years before. It should be added that uniformly positive results followed a series of tuberculin tests made according to the method of von Pirquet.

Although negative evidence is of comparatively little value as compared with positive findings, I cannot refrain from referring briefly to a second case of this affection which has been under my close observation for a period of four years. The patient is a robust man apparently in excellent health, apart from his cutaneous disease, about 50 years old, and his disease has lasted seven or eight years. It occupies and is limited to both cheeks. The eruption is quite florid

1. Barber: Brit. J. Dermat. **27**:365, 1915.
2. Barber: Brit. J. Dermat. **31**:186 (Oct.-Dec.) 1919.

in appearance with a moderate amount of infiltration, especially about the borders. A recent roentgen-ray examination by one of the most skilful roentgenologists in the country and a thorough inspection by a competent dentist have failed completely to disclose any disease of the teeth. A thorough examination of the throat and especially of the tonsils has disclosed nothing abnormal; the tonsils are quite small and are completely hidden between the pillars of the fauces. The patient is positive in his statements that he has never had any trouble with his throat. In conclusion, it may be stated with confidence that there is no disease of either teeth or tonsils, and that there have never been any symptoms suggesting the presence of focal infection elsewhere.

Truly, "experience is fallacious and judgment difficult."

DISCUSSION

DR. PUSEY recently had a case analogous to Dr. Hartzell's which suggested the possibility, as Dr. Hartzell's had, of the causal relationships of focal infection to some cases of erythematous lupus. This case was that of a young woman with severe erythematous lupus of long standing on the face, the patches showing a good deal of infiltration and thickening; they were elevated and of a dark chronic red color. This woman's teeth had been found to be in bad condition, most of them showing alveolar abscesses, for which removal had been advised. On the removal of the teeth there was a temporary exacerbation, but in the course of a month there was distinct improvement. Two months later the improvement continued. He was glad that Dr. Hartzell had called attention to this possible factor in erythematous lupus, but, like Dr. Hartzell, he thought that focal infections were only one of the many sources of intoxication that might produce erythematous lupus.

DR. SCHAMBERG wished informally to place on record another case of acute fulminating erythematous lupus. The patient was a woman, about 40 years of age, with an ordinary lupus erythematosus on the face, who developed an erysipelatoid appearance of the facial lesions, new patches on the body, and in whom a pneumonic consolidation with high fever caused death in a few days. Unfortunately, he was unable to obtain a necropsy examination.

In regard to the work of Barbour, which had been quoted, we should certainly be extremely reserved about accepting any direct relationship between the streptococcus and lupus per se. He did not think anyone had succeeded in establishing fixed types of streptococci which had specific pathogenic effects. Some years ago he made cultures of the throats of 100 patients with scarlet fever and these were bacteriologically studied by Dr. Gildersleeve, who found 92 per cent. of streptococcus in these throats. Cultures were then made from 100 apparently healthy university students in whom 82 per cent. showed the streptococcus, and these killed guinea-pigs with as much rapidity as those rrom the throats of the scarlet fever patients. Furthermore, the streptococcus was present in the throats of most persons.

In regard to the improvement which occurred in one of the reported cases of lupus erythematosus from vaccines, it was possible that this was the effect of a nonspecific protein. It was well known to dentists that exacerbation of symptoms for which the patient sought relief often temporarily followed the

extraction of incriminated teeth. This is believed to be due to absorption of organisms from the vascularized infected focus. It is conceivable that an absorption of nonspecific organisms might also bring about improvement.

DR. WALLHAUSER reported a case which terminated fatally. The patient was a woman who had developed an eruption over the bridge of the nose which extended out over the cheeks; this had persisted for about one year—the color was a deep purplish red with superficial scaling. The resemblance to lupus erythematosus was striking, but some of the characteristic features of this condition were lacking—elevated border, atrophy, etc. Febrile symptoms were present, the temperature ranging from 99 to 104 degrees. A focal infection was carefully considered and every effort made to locate the source, with a negative result. The patient gradually passed into a state of coma and died; the postmortem examination revealed an abscess of the liver.

DR. FORDYCE agreed with Dr. Pusey that lupus erythematosus might have a multiform etiology. He was convinced that a certain percentage of cases were related to tuberculous foci somewhere in the body. He had reported, at a former meeting of this association, a case of lupus erythematosus of the face in which a tuberculous focus was found in the kidney at necropsy. He had seen numerous cases of lupus erythematosus with coincident tuberculous lymph nodes in the neck. In one of these cases, after an operation on the lymph nodes, numerous patches of lupus erythematosus appeared on the face. Years ago Dr. Fordye reported symmetrical patches of lupus erythematosus on the hands and forearms of a pregnant woman who developed convulsions before her confinement. The lupus erythematosus disappeared after her confinement.

DR. MCEWEN said that as the subject of focal infection was almost certain to occupy increasingly the attention of dermatologists, he wished to mention two points. First: Is one warranted in saying that the tonsils are not foci by simply saying that they do not appear to be, because they are buried and small? He knew of a case in which there were pronounced joint symptoms; when the small, fibrous, and deeply buried tonsils were taken out they were found to contain visible pus. Second: In looking for foci the gall tract should not be forgotten. The gallbladder and ducts are often the seat of a chronic infection which may become focal in effect, but the profession is so prone to think of the teeth and tonsils as the only foci that this fact is apt to be overlooked.

DR. CORLETT stated that he had always been of the opinion that lupus erythematosus was not associated clinically with tuberculosis or lupus vulgaris. He never yet had seen a case of lupus erythematosus associated indubitably, other than by family history, with lupus vulgaris or tuberculosis. About a year ago, however, when Dr. Stokes presented his valuable study relative to foci of tuberculosis giving rise to or associated with lupus erythematosus, he realized that many cases might harbor foci of tuberculosis that were not demonstrable by ordinary examination or apparent from visual inspection. That lupus erythematosus was caused by other agencies and that reflex nerve irritation might be a potent factor in its causation Dr. Corlett had also believed. The latter belief was borne out by certain observations; one he especially recalled, made a number of years ago, in a woman who was a stenographer, whose eyes had been corrected by some traveling optician and who had a very extensive lupus erythematosus, not of the ordinary butterfly form, but surrounding the palpebral region. A careful examination of the eyes by a skilled oculist and proper glasses brought relief in the course of some months, so that the ordinary applications that had been useless before were effective in producing a cure.

Again, as a possible cause of lupus erythematosus, foci of infection may be encountered in the teeth, as evidenced by two cases of herpes in a woman whose teeth were in a very bad condition and whose mouth was a source of irritation, reported last year before this Association. After the teeth were put in proper condition or extracted, no attack of the skin manifestation took place and finally, after some months, the cutaneous symptoms all disappeared.

Since that time Dr. Corlett had had a case of inflammation of the cheek which resembled a circular patch of eczema and which was very obstinate to treatment. Various applications had no effect. This woman received numerous roentgen-ray examinations, and well defined abscesses were found. These were removed and the mouth properly treated. In the course of a few weeks the lesion on the cheek began to heal and in due course finally disappeared.

Dr. Corlett wished, however, to give a word of warning against extracting teeth indiscriminately. The average practitioner, reading a report of this sort, was apt to think that everything dermatologic was due to infected teeth, and during the last few years there had been more sound teeth extracted than one would think possible. He felt that the profession should be on guard against attributing indiscriminately various infections to the teeth, although they must also recognize that such an infection was often effective in producing various disorders.

Dr. Highman thought the question raised by Dr. Hartzell's presentation was of tremendous importance in relation to such a clear cut condition as lupus erythematosus. It should be borne in mind that one was dealing with a distinct clinical entity. When the question of etiology came into consideration, one was at once confronted with the fact that here again was an example, in a very restricted manner, in which tissue was able to respond uniformly to various pathogenic causes. He had seen one case which in one way was a parellel with Dr. Hartzell's and in the other was like the cases brought out by Jadassohn. The case was that of a woman of about 20 years of age who for six or eight months had had malaise and weakness. She developed a patch of lupus erythematosus and complained of a peculiar, bandlike headache. Dr. Highman sent her to an otolaryngologist, who found an empyema of the antrum of Highmore. Under treatment of the latter, the lupus erythematosus began to disappear. Whether this was an example of focal infection in lupus erythematosus, he did not know. He was not a focal infection "fan," for every nook and cranny of the body might contain a bit of pus and he did not believe that every disease such a patient had must arise from that focus. Nevertheless, it did seem that when a condition of this sort was present, and when after the removal of the focus it disappeared, that there must be some relation.

Dr. Highman had seen some cases connected with tuberculosis. The whole literature was full of such cases (Jadassohn). Kyrle reported lupus erythematosus on one cheek and lupus vulgaris on the other. Everyone had seen lupus erythematosus associated with papulonecrotic tuberculids, and even some lesions in the Darier-Roussy type of sarcoid had distinctly the clinical appearance of lupus erythematosus. There was no getting around these facts. Thus there seemed to be some connection between lupus erythematosus and tuberculosis.

Dr. Stokes had seen within a comparatively short time two cases with extensive erythematous lupus of the face which had completely recovered for the time being following erysipelas. The patient had apparently experienced

a kind of fortuitous vaccine therapy. One should be particularly careful not to allow such observations to lead him into unwarranted conclusions as to streptococcal etiology.

With reference to an association with tuberculosis, he had seen many striking instances of it. His study of the association of streptococcal foci with tuberculids had led him to offer the hypothetical suggestion that cutaneous sensitization from a pyogenic focus might serve as a secondary etiologic factor in the production of erythematous lupus with tuberculosis as a primary etiology or the reverse. In this way erythematous lupus might be regarded as a toxic or allergic manifestation of associated tuberculous and streptococcal focal infections.

DR. HARTZELL (closing) emphasized the fact that while it was not common, erythematous lupus occasionally disappeared spontaneously, a fact which made it difficult to decide as to the action of any particular remedy. He had seen two cases of that sort. If he had given the impression that he was arguing for an etiologic relationship between erythematous lupus and focal infection, he had given the wrong impression. It was not his purpose to argue either for or against such a relationship; he simply wished to report a case which impressed him very much on account of the improvement following the removal of the teeth.

As to the multiform etiology of erythematous lupus, that might be true, but he disliked very much that sort of conclusion about disease—it seemed to him a sort of compromise. It was true that a number of diseases have a multiple origin, but before deciding anything in that respect, one should be quite sure of it.

XV. TREATMENT OF GENERALIZED PSORIASIS*

WILLIAM H. MOOK, M.D.
ST. LOUIS

When the idea to present a paper on the treatment of this disease came to mind the subject seemed simple enough, but a consultation with the literature soon convinced me that a textbook on the subject was more in order than a paper, so the title more properly should have read: "A Note on Another Method of Treating Generalized Psoriasis."

Intelligent people suffering from the disease learn within a comparatively short time to carry their handicap with little trouble, but its presence is always a handicap, ever demanding more or less embarrassing explanations on its discovery by another person. This was especially true in army life.

Apology may be made for the severity of the course to be outlined, but since the necessity in war developed the method it may prove of future value until the specific or a more rapid method is discovered. The etiology being unknown a specific for its eradication, temporary or permanent, is wanting. It would of course be folly to suggest any line of treatment that would produce favorable results in all cases or varieties, for we well know the resistance to all forms of treatment of the parasoriasis group, as well as individual cases of the ordinary typical psoriasis.

It is not my intention to discuss the various remedies, drugs, diets, or electrically generated methods—they all have their place and are valuable—but to present to you a new combination with an old, and in our opinion, the best drug for the removal of the lesions in generalized cases, namely, chrysarobin. Most patients with a few, or frequently with many lesions, are more or less indifferent to their presence, but when the lesions become generalized and unsightly and manifest subjective symptoms a radical course of treatment is necessary.

In 1904 the author learned the treatment of generalized cases with the Dreuw ointment and up to a short time ago we have relied on it, but in 1918, while with the American army in France, two weeks were spent in the largest British skin hospital at Hardelot, France, observing their methods of treating diseases in soldiers. There were four expert

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* Studies, reports and observations from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., Service of Drs. M. F. Engman and W. H. Mook.

* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

dermatologists under Lieut.-Col. Henry MacCormac of London, treating from 1,500 to 2,000 skin patients most of the time. During my stay of two weeks in February there were about eighty patients with psoriasis, most of them with profuse lesions. It is to Dr. H. W. Barber of London, a member of the staff at that time, that I am indebted for the formula presented in this paper. Since saving of man power was absolutely necessary, time was the most essential factor in treatment. Barber informed me that he had experimented with many drugs and had finally evolved a formula of 2 per cent. phenol and 10 per cent. chrysarobin in petrolatum as the best combination. He had read somewhere that phenol enhanced the action of certain drugs and on trial with chrysarobin he was able to reduce the hospital stay of soldiers suffering from psoriasis. Since my return last June we have had such marked success in cutting down the duration of treatment that it is thought advisable to publish our method in detail.

The patient is informed that he must go to a hospital or be confined to his home under the care of a nurse for a period of from twenty to twenty-five days. He must be visited daily. Owing to the danger of chrysarobin dermatitis, as well as destructive action of chrysarobin on clothing and bed clothes, confinement to a room or hospitalization is necessary. Three ointments are used, the amounts of the drugs to be varied to suit individual reactions and idiosyncrasies.

TREATMENT OF SCALP, FACE AND HANDS

Salicylic acid and white precipitate of mercury, 5 per cent. each, in white petrolatum, is to be rubbed into the scalp once daily. The percentage of the drugs may be increased cautiously. If lesions exist on the hands or face half these strengths may be used. Tar ointments may be used in patients with an idiosyncrasy to mercury.

TREATMENT OF THE BODY

Two ointments are necessary—one to prevent as much as possible and to relieve, the chrysarobin dermatitis. First a soothing application is used: 1 per cent. ichthyol (or a substitute), corn starch and zinc oxid, 6 per cent. each, in white petrolatum. This is to be applied to the normal skin between patches before the chrysarobin ointment is applied. It is also to be used after the chrysarobin dermatitis has developed. Second, a chrysarobin ointment, which consists of 2 per cent. phenol and 10 per cent. chrysarobin in white petrolatum, is applied. These amounts will be advantageous in a majority of cases, but may be decreased or increased when advisable. The patient should be warned of the danger of conjunctivitis from chrysarobin and instructions given to prevent its occurrence.

After the ichthyol or soothing ointment has been applied to the normal skin between the lesions, preferably with a wooden tongue depressor or spatula, the chrysarobin ointment is applied to the lesions with a swab made of cotton or gauze twisted on the end of a stick. Stiff brushes are to be avoided as too irritating. Corn starch or talcum powder is then dusted plentifully over the entire body and the patient advised to abstain from walking or exercising as much as possible, though it is not necessary to remain in bed. Bandaging the extremities is not necessary and causes discomfort. A large arm chair in the room will add to comfort.

Applications are made once daily until the chrysarobin dermatitis begins to develop, and it is at this point that the greatest skill in the treatment must be manifested. The chrysarobin must be discontinued if severe reaction develops. An occasional corn starch and soda bath may be advisable as a rest and for cleansing purposes, using two cups of starch and one cup of baking soda to the bath tub full of warm (not hot) water.

The skin will be discolored after the first treatment and after three to six days the skin generally becomes much reddened, but with less real inflammation than is usual when chrysarobin alone is used. The ointment is not to be discontinued unless the distress from burning and pruritus is unbearable. If the chrysarobin must be discontinued for a few days, the soothing salve is applied twice daily until it may be resumed. In some patients the chrysarobin may be applied continuously until all lesions have disappeared. In a few, two applications daily are possible, but in a majoirty rest is indicated after five or six days. Occasionally persons with idiosyncrasy will be encountered and in these the method is useless.

SKILL NECESSARY IN USING THIS METHOD

The objections to the method are many and individual skill must be developed. Certainly it is a dangerous weapon for the unskilled. The confinement to a room or hospital, the destruction of a certain amount of clothing and the physical discomforts that may be encountered are obvious, but when necessity or desire demands a rapid removal of lesions with a favorable assurance of success, we can heartily recommend it.

DISCUSSION

DR. SCHAMBERG said that the action of chrysarobin on the skin appeared to depend on three factors: First, its powerful reducing effect; second, its marked affinity for the keratin or epithelial tissues, and, third, its relative stability or the slowness with which it undergoes oxidation. The stain cannot be removed from the epithelial cells by boiling with strong acids or alkalies. When it becomes oxidized it develops into chrysophanic acid, which is therapeutically relatively inert.

Every one realizes that drugs like chrysarobin have a great influence on the lesions of psoriasis. It is a common observation that in the acute developmental stage of the eruption drugs like chrysarobin often cause a spreading or extension of the eruption. He believed there were three stages of the disease, the developmental, the quiescent and the stage of spontaneous decline. If the disease was attacked in the active developmental stage with arsenic internally or chryasorabin externally, harm was commonly done, but these drugs during the quiescent stage had a marvelous effect on the eruption. Was there any way of converting the developmental stage into the stage of quiescence? Dr. Schamberg thought two procedures were of value for this purpose: first, the use of a low protein diet and, second, the administration of autoserum injections. He had recently had two most rebellious cases of psoriasis in which no active remedies could be used without doing harm, but after the use of several autoserum injections the active stage of the disease was rendered quiescent and the drugs that could not be tolerated before could be tolerated and were highly efficient in bringing about an almost complete disappearance of the eruption.

Dr. Engman asked what was the peculiar action of the psoriasis itself between the white halo and the surrounding skin which became pigmented.

Dr. Schamberg, replying to Dr. Engman, said he did not think the reason for this was known. Every one had observed, he was sure, in psoriasis patches treated with chrysarobin a small halo, perhaps a quarter of an inch in width, around the psoriasis patch, which failed to take the stain, owing to some peculiar feature of this border area and the lack of affinity between the keratin at this margin and the chrysarobin.

Dr. Grindon stated that the white halo around the patches had long interested him. He had long thought that the explanation just given by Dr. Schamberg was the correct one, but he had changed his mind, when he observed the same white halo around the patch when dermatitis was excited by the Kromayer lamp as when chrysarobin was used. The cause evidently lay in the skin itself and not in the agent employed.

As to the use of chrysarobin, Dr. Schamberg was right in saying that it was harmful when used in the active stage of the attack. Dr. Grindon believed that we often made a mistake in using chrysarobin in too great strength. He was at one time fond of using the Dreuw ointment. There was no doubt but that chrysarobin would clear up many cases, but new lesions were sometimes provoked by the dermatitis. He did not now use it stronger than 2 per cent. and in most cases obtained as good an effect as from the stronger ointment. There was a simple method which gave as good results as any other in chronic and refractory cases. Patients take two baths a day, at a comfortable temperature, remaining in the bath perhaps an hour each time, with half a pound of sodium bicarbonate in the bath. Results were not striking, but neither were they by other methods, and this was as good as any.

Dr. Irvine thought that whatever the etiology of psoriasis, we must recognize that many factors serve to aggravate it and bring on attacks. In a generalized psoriasis more could be done by directing the conduct of patients along the lines of general hygiene than by the particular use of any one drug. His patients had shown more improvement from this than from any other method. The improvement of bad hygiene and improper diet had a good effect. Dr. Irvine thought it was also well to emphasize the hospitalization. Much more could be done for generalized psoriasis by putting the patients to bed where

their habits could be controlled than by using any combinations of or single drugs in treating the skin. In his opinion, this was of such great importance that he tried to use those drugs that were the most satisfactory to the patient, namely, those easiest and pleasantest to use. He found in his patients that with the use of a daily bath and a simple ointment, such as salicylic acid and sulphur, and putting them to bed they got along just as well as with something disagreeable like chrysarobin, the dirty tars or other things of a like nature.

Dr. Highman said that the discussion of the treatment of psoriasis always stimulated oratory and every one had a series of experiences that never seemed to jibe with those of his colleagues. In rendering the lesions quiescent in the sense brought out by Dr. Schamberg, Dr. Highman did not understand the relationship of diet to the matter, or that of autoserum. His own experience, so far as low protein diet was concerned, could be illustrated by examples. One case was that of a woman of 40 or 45 with generalized psoriasis extending from the ankles to the shoulders. She had been on a rice diet for six months and had become despondent, largely through starvation. When she was put on a bland mixed diet the lesions on her body began to involute rapidly. The local therapy was 2 per cent. salicylated petrolatum. He had never seen that formula accomplish anything in psoriasis before, but he had to use something to keep the skin pliable because it was practically lichenified all over the body. The same thing was illustrated in a clinic in New York. A young woman came in and the doctor said, "I want you to stop eating meat and eggs," to which the patient replied, "I have never in my life eaten either." These things were difficult to reconcile.

Dr. Howard Fox was much interested to hear Dr. Schamberg's reference to autogenous serum injections. He had had no further experience with this procedure for the past few years. In regard to the chrysarobin treatment of psoriasis, he wished to call attention to the value of impermeable dressings to cover the chrysarobin applications. This plan was generally known but seldom followed. In some obstinate cases he felt that the action of the chrysarobin was greatly increased by covering the skin with oiled silk or rubber cloth, which prevented the evaporation of sweat and caused maceration and softening of the scales. It was on this principle that entire suits of similar materials had been previously employed by some of the dermatologists of Vienna.

Dr. Towle was of the opinion that the intensity of the symptoms could be much mitigated by diet. Last year they carried out a number of series of experiments which corroborated it in every detail. In addition to that, as was mentioned by Dr. Grindon, prolonged hot baths, sometimes prolonged, one, two or three hours, were given and under these conditions chrysarobin was found to be more effective. The heat unquestionably had something to do with it. Another method of mitigating the intensity of the eruption in patches that were not too large was the application of crude coal tar, which would dry lik gutta percha. Some quite remarkable results had been achieved with that method. The cutting down of the diet seemed to enhance the action of the drugs. There was an old-fashioned remedy—the internal administration of potassium acetate—formerly used in connection with chrysarobin. This was sometimes useful.

Dr. Hartzell asked Dr. Mook whether he ever observed any evidence of phenol poisoning. In his opinion the application of a 2 per cent. ointment was not free from danger. He cited a case of universal psoriasis seen a year or two ago in which, according to the patient's statement, a daily dose of 10 grains

of sodium cacodylate had been given hypodermically for an entire year with no untoward result; during this time the eruption had almost completely disappeared.

Dr. Haase recalled the fact that he spoke several years ago of the use of crude coal tar, straight from the gas house, in treating psoriasis. He had obtained good results from that treatment. In one case he applied it to a generalized psoriasis and the lesions cleared up, but in a short time the man had an albuminuria and he feared that was due to the application of tar all over his body. So he was now limiting the use of straight-run crude coal tar to localized patches of persistent psoriasis.

He had recently had an interesting experience in a young boy with reference to the use of phenol. The boy had a persistent, ugly patch on each knee. On one knee he had a rather deep-seated furuncle. The surgeon used a 2 per cent. phenol ointment on the furuncle and the patch of psoriasis. With the disappearance of the furuncle the psoriasis disappeared. When tried on the other knee it had no effect.

Dr. Wile thought there was no doubt that Dr. Mook saw the marked improvement under the method described, but a point had occurred to Dr. Butler and himself—had not the rapid improvement been due largely to the fact that he hospitalized the patients? Most of the patients were ambulatory and in many instances when they were persuaded to come into the hospital for treatment, the mere fact that they remained in bed and devoted the greater part of their time to the treatment greatly shortened an attack. He wished to know whether Dr. Mook did not agree to this.

Dr. Wise believed Dr. Mook's paper referred chiefly to soldiers treated in the army and the discussion was more directed toward treatment of psoriasis in general. He knew that Dr. Mook had used Dreuw's ointment.

Another question he wished to ask was whether the addition of salicylic acid would increase the efficiency of the new formula?

One thing that had not been mentioned was the roentgen ray. Dr. Mook had stated that it took twenty-five days to clear up the average eruption, which was the average time for any psoriasis without the application of an ointment, and without the inconvenience and staining associated with the use of chrysarobin.

Dr. Hazen recalled two cases of generalized psoriasis that lasted all winter in spite of most of the treatments mentioned and when the bright, sunny days of spring came both patients became well within two weeks.

Dr. Smith was interested to know whether others had noted this condition. A young woman who had had a mild psoriasis for several years showed an acute exacerbation at the height of which she developed an acute attack of tonsillitis, and the psoriasis practically disappeared. The complete resolution of the lesions was rapid and as far as he knew there had been no recurrence. This might be simply a coincidence.

Dr. Stokes thought hospitalization was a prominent factor in the improvement of patients, largely because they devoted nearly all their time to treatment. He had found that if he could induce a psoriatic patient to spend even a week in the hospital he could greatly increase the efficacy of treatment.

Dr. Fordyce thought it more important to have a committee appointed to standardize the treatment of psoriasis than of syphilis. He had one or two suggestions to offer. One was the use of a 30 to 50 per cent. ammoniated mercury ointment in psoriasis of the scalp and face. The lesions yielded more

rapidly to an ointment of this strength than to the one usually employed. Occasionally mercurial stomatitis followed its use. He said that better results would be obtained if chrysarobin ointments were applied by a trained nurse or by some one familiar with their use. When the applications were entrusted to the patient alone, they were not as a rule used in a manner to bring about the best results. It was important in treating patches of chronic psoriasis to produce a decided reaction in and about the lesions. It was furthermore important in his opinion to cure all of the lesions, as by so doing relapses would probably be less frequent.

DR. VARNEY expressed the opinion that the paper had offered some valuable suggestions, and in speaking only of generalized psoriasis, which all had trouble in relieving, he emphasized the sunlight treatment that Dr. Hazen had just mentioned. At this time of the year we can get a welcome relief for rebellious psoriasis patients by prescribing sunlight in a definite way. He was more likely to tell a patient to get into B.V.D.'s and a canoe and spend a given length of time, increasing this each day, in the sunlight on the water between 11 and 2 in the day time, as he was to prescribe any local drug treatment. He believed this would do more toward clearing up a large percentage of generalized psoriasis than any other form of local treatment. From the last two weeks in May until the middle of September, we have the most direct chemical sun rays, if they can come through clear air instead of the smoke screen that hangs over our cities.

DR. ENGMAN said he had observed the treatment that Dr. Mook had learned in France, and he thought it the most rapid treatment he had yet seen. One little therapeutic sign that he had found of value was brought out by Dr. Schamberg, who spoke of the difference in the degrees of the different stages of psoriasis. They found that in acute attacks and in chronic persistent attacks a systemic shakeup was a good thing. Some years ago, in experimenting with foreign proteins in various diseases, they found that psoriasis could be eradicated by bringing up a high temperature by doses of foreign proteins. Just why this was the case he did not know. They had been using typhoid vaccine and by injecting a dose every four days the psoriasis would usually begin to disappear quite rapidly. A change occurred and then by applying chrysarobin or some other drug and giving the patient a hot bath it seemed to increase the effect of the drug. Dr. Engman had never seen this method cause an attack of psoriasis to disappear, but he had seen it assist materially in other forms of treatment.

DR. MOOK (closing) said that early in his dermatological career he had a sad experience with psoriasis. While in the Skin and Cancer Hospital in New York a young man came in with a generalized distribution of this disorder and he had just learned about the treatment with Dreuw's ointment. The scales in this case were so thick that he conceived the idea that a good way of getting rid of them in a hurry would be to put on green soap for about half an hour. This was done and he then advised the application of Dreuw's ointment all over the body. In half an hour the patient was unconscious and the only symptoms to guide him were profuse perspiration and rapid pulse. He finally made a diagnosis of salicylic acid poisoning. The symptoms of severe poisoning persisted for thirty-six hours, but the man finally recovered.

In regard to the treatment of generalized psoriasis, every one knows about using chrysarobin only in the quiescent stage. In the British army, with eighty or 100 cases all the time, they showed that most patients could be treated with chrysarobin even in the developmental stage. Barber had been experimenting

with psoriasis for three or four years. It was troublesome and with somewhere around 100 men in the hospital all the time from this disease it was serious in loss of man power to the British army. Since his return to private practice he had been putting practically all his patients on this ointment. Years ago he used the unequaled Dreuw ointment in practically all cases. He believed, in treating a large number of patients with large lesions, the stronger ointment was necessary to produce a dermatitis and chrysarobin reaction. If it can be controlled just short of the intense burning and itching the lesions disappear more rapidly than without the reaction.

The point brought up by Dr. Engman was a very striking one at that time and they saw lesions of generalized psoriasis almost disappear in seven or eight days, but if the patient was left alone inside of two or three weeks they would reappear. In the treatment of generalized cases, they found that it was better to remove every single lesion on the body and Dr. Mook thought this was important, especially about the scalp, elbows and knees. The chances for early recurrence were thus much lessened.

He used radiotherapy in a few selected cases. One of the first things they do at the Barnard Skin and Cancer Hospital is to teach the patient as much as possible about this disease. He had taught many patients to use Dreuw's ointment and most of them knew the treatment and their individual reaction as well as Dr. Mook did, and carried out the treatment themselves.

Dr. Wise had asked about the comparison of the new treatment with the Dreuw ointment. Dr. Mook had four patients whom he tried out, formerly treated with Dreuw's ointment. Some patients come once a year or every two or three years. When they developed a profuse eruption they would come in and stay in the hospital until they were well. The average time for acute cases of psoriasis under the Dreuw ointment treatment was from five to six weeks. With the new treatment this had been reduced in one case to nineteen days, in one to twenty-one days, and in one to twenty-four days, so the matter of a reduction of two weeks in the treatment was quite important for army purposes. The treatment was dirty and it was difficult to put patients in the hospital, but if they went they recovered from their psoriasis.

In regard to hospitalizing and rest in bed, there was no doubt but that rest would change the condition of the psoriasis as well as in many other skin affections. So far as attempting to remove psoriasis in a short time was concerned, the rest would not do it.

In regard to phenol poisoning, Dr. Barber said he had treated many cases and watched the urine carefully, but he had never seen any phenol poisoning or albumin in the urine following the use of this treatment.

Radiotherapy may be used over certain areas of the body, but it is rather a dangerous procedure unless one is well trained in the use of the Coolidge tube, with massive doses, and he thought it would be dangerous in cases of psoriasis to repeat this treatment every three or four years in succession.

This treatment only referred to those who had severe symptoms and wanted to get rid of the eruption in a short time.

A MENACE IN THE LOW PROTEIN DIET*

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Since the investigation of Schamberg[1] and his collaborators on protein metabolism in psoriasis and the distinctly beneficial results obtained by them in this disease by restricting the nitrogenous intake, it has become more or less a routine with a great many dermatologists to place patients with psoriasis on a low protein diet. The use of such a diet has not been confined to psoriasis; it is being advised in a number of other dermatoses—dermatitis, to instance one.

In reducing the protein intake, the caloric requirements are made up usually by that of carbohydrates and fats. Practically, the increase occurs most often in the carbohydrate components, since they are more agreeable to the majority of patients. A diet of this kind, rich in starches and sugars and poor in proteins, may be kept up for a long time, either by order of the physician or by the patient's own volition.

It is not my intention to discuss the value or uselessness of this diet; but owing to its widespread adoption, it becomes of importance to call attention to a possible danger, and thus, to a contraindication to its use, in certain patients.

Diabetes is recognized universally as a contraindication to a diet rich in carbohydrates; but it is not so generally realized that there exists a detectable prediabetic state in which a diet of this type sooner or later leads to permanent glycosuria. To continue a prediabetic patient on a diet composed of large amounts of carbohydrates is tantamount to condemning that person to diabetes. Two cases recently under observation exemplify these points.

REPORT OF CASES

CASE 1.—Miss B., aged 22, first seen May 6, 1920, had psoriasis which began six years ago. In June, 1917, she had an acute, generalized attack. At this time she was treated with fractional doses of roentgen ray and placed on a restricted protein diet. The eruption wholly disappeared, but recurred in April, 1920, a few patches presenting on the scalp, elbows and thorax. For two and one-half years she remained on the diet first prescribed, because she was told that it might prevent recurrence. Her diet consisted mainly of potatoes and bread, smaller quantities of coarse vegetables and a small piece of meat every other day.

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* From the Department of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University, New York.

1. Schamberg, J. H.; Ringer, A. I.; Raiziss, G. W., and Kolmer, J. A.: Summary of Research Studies in Psoriasis, J. A. M. A. **63**:729 (Aug. 29) 1914.

She was overweight and flabby, with a pale, pasty complexion and puffiness about the eyes that suggested a diabetic habitus. There was complaint of polydipsia, polyuria and nocturia. A general physical examination was negative except for a persistent pulse rate of 100.

June 17, 1920: Urinalysis showed no sugar.

June 24, 1920: A glucose tolerance test gave the following result: blood sugar (before glucose), 0.142 per cent.; urine sugar, negative.

10 a. m.: Glucose, 100 gm., in 200 c.c. water.

	Percentage of Blood Sugar	Urine Sugar
10:30 a. m.	0.344	Positive
11:00 a. m.	0.300	Positive
12:00 m.	0.248	Negative
1:00 p. m.	0.178	Negative
2:00 p. m.	0.162	Negative

Marked nausea continued for twenty-four hours.

This test showed a prediabetic state of advanced grade. The appearance of glycosuria was particularly ominous and definitely pathologic. It was evident that a diet rich in carbohydrates was strictly contraindicated. The diet, therefore, was changed to conform to the findings, and the psoriasis treated with roentgen ray, under which it has cleared up except on the scalp.

July 8: Blood sugar, 0.140 per cent.; urine sugar, negative. She was still hyperglycemic, which if persistent, indicates the need of fast days.

This case exemplifies three important facts: (1) the inadvisability of instituting a diet rich in carbohydrates without previous knowledge of the patient's ability to take care of it; (2) that absence of glycosuria is not always an index of safety; and (3) that a glucose tolerance test may indicate a state of grave danger to the patient, which may be aggravated unwittingly by a rich carbohydrate diet, such as is usually instituted when psoriatic patients are placed on low protein intakes.

Case 2.—Mr. E., aged 24, first seen June 8, 1920, had a widespread seborrheic dermatitis which had been present for many years. At present it was severe on the scalp, face, arms and thighs. There have been occasional remissions but never complete freedom. He had been treated by various means for years without avail. Two years ago he was placed on a low protein diet and had voluntarily continued it since. He subsisted principally on coarse vegetables and starchy foods. During the first year of this diet, he took no animal food; for the past twelve months he had eaten an occasional piece of beef or chicken.

In an endeavor to discover an etiologic factor, a glucose tolerance test was performed. The results were: blood sugar (before glucose), 0.093 per cent.; urine sugar, negative.

10:15 a. m.: Glucose, 100 gm., in 200 c.c. water.

	Percentage of Blood Sugar	Urine Sugar
10:45 a. m.	0.264	Negative
11:15 a. m.	0.188	Negative
12:15 p. m.	0.176	Negative
1:15 p. m.	0.166	Negative
2:15 p. m.	0.162	Negative

He had no nausea.

Lowered glucose tolerance is well demonstrated in this test. Glycosuria did not occur, but the failure of the blood sugar to return to a normal figure inside of four hours is significant of lowered sugar assimilability. It can be assumed that this patient would be injured by a persistently high carbohydrate intake; perhaps eventually to a stage of pancreatic hypofunction leading to permanent glycosuria. Certainly the diet that had been advised for the seborrheic dermatitis was contraindicated in view of the potential diabetes elicited by the glucose tolerance test. He was, therefore, placed on a diet conforming to this finding.

REMARKS

The important point is the detection of the potential diabetes; when that has been ascertained the physician becomes master of the situation. Should he elect to continue a low protein diet, it is possible, in most cases, to achieve his purpose, and still maintain a carbohydrate and protein intake consonant with the conditions confronting him. By frequent blood sugar estimations, a record can be obtained, which will determine whether the campaign is to be maintained or abandoned. Prediabetic patients should be told of their condition, its control and dangers, so that they do not unknowingly adopt a diet which is fraught with danger to them.

The question whether a rich carbohydrate diet can, of itself, cause diabetes is still sub judice. Experimental evidence apparently shows that this disease can be produced only when a latent tendency toward it already exists. No amount of sugar feeding to normal animals causes diabetes in them; but animals which by operative procedures have been rendered latent diabetics, may develop the condition by overfeeding with saccharin substances. Allen [2] believes that the increase of diabetes in civilized peoples is due to the stirring up of a latent tendency by a combination in which mental stress and rich carbohydrate diet are the principal elements.

CONCLUSIONS

1. Most patients, on a low protein diet, receive an increased carbohydrate ration.

2. Allen, F. M.: Glycosuria and Diabetes, Cambridge, Harvard University Press, 1913, pp. 592 and 1062.

2. A diet rich in carbohydrates is contraindicated in patients who present a prediabetic condition.

3. Patients who have psoriasis or other dermatoses, in which a low protein diet is often resorted to, may also be prediabetics.

4. Therefore, before a special diet, low in protein and rich in carbohydrates, is instituted, the sugar tolerance of the patient should be ascertained.

Thanks are expressed to Prof. John A. Fordyce for his permission to use the facilities of the Laboratory of the Department of Dermatology and Syphilology, Vanderbilt Clinic, New York.

THE USE OF GENTIAN-VIOLET AS A RESTRAINER IN THE ISOLATION OF THE PATHOGENIC MOLDS

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The work of Churchman [1] on gentian-violet has shown that this substance possesses the peculiar property of inhibiting in high dilution the growth of grampositive organisms. This fact has been confirmed by Krumwiede and Pratt,[2] and applied by Petroff [3] in his medium for isolation of cultures of the tubercle bacillus from sputum. As most of the skin saprophytes are gram-positive, it occurred to us that gentian violet might be of value in restraining the growth of skin contaminants in cultures during the isolation of the pathogenic molds of the skin and hair, provided the substance should prove to be non-inhibiting for the molds themselves.

AUTHOR'S EXPERIMENTS

Technic.—A preliminary series of experiments was undertaken using four molds of widely varying growth characteristics to determine in a general way the effect of gentian-violet on their growth. The organisms, all of which were isolated in this laboratory, selected were: (1) *Penicillium* (*saprophytic*), (2) *Achorion schönleinii* (D. R. 206), (3) *Trichophyton rosaceum* (D. R. 201), (4) *Microsporon audouini* (D. R. 73). A 1-100 watery solution of gentian-violet (Grübler) was carefully prepared. This was added to tubed Sabouraud's maltose mediums (melted 10 c.c. to each tube titrated to 1 per cent acid, phenolphthalein) so as to make these dilutions: 1:1,000,000; 1:500,000; 1:400,000; 1:300,000; 1:250,000; 1:200,000; 1:166,000; 1:143,000; 1:125,000; 1:111,000; 1:100,000; 1:83,000; 1:71,000; 1:60,000; 1:58,000; 1:41,000; 1:20,000; 1:10,000; 1:5,000; 1:1,000.

The tubes were seeded and allowed to incubate at room temperature for four weeks. Slants of Sabouraud's maltose agar not containing gentian-violet were seeded as controls.

Results.—1. *Penicillium* grew through all concentrations abundantly and with no evident impairment except in the two strongest

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

1. Churchman: J. Exper. Med. **16:** 1912; Churchman and Michael: Ibid.
2. Krumwiede and Pratt: Centralbl. f. Bakteriol. **68:** 1913; Ibid., Proc. New York Path. Soc. **13:** 1913.
3. Petroff: Johns Hopkins Hosp. Bull. **26:**276 (Aug.) 1915.

(1:1,000 and 1:5,000), in which the growth was well developed but somewhat less vigorous than in the control.

2. *Achorion schönleinii* grew up to a concentration of 1:71,000. No growth occurred in greater concentrations. It was abundant through 1:100,000 with no evident inhibition as compared with the control on the next two tubes. The growth graded downward in vigor until it was scanty on the tube representing a dilution of 1:71,000.

3. *Trichophyton rosaceum* grew through 1:41,000. Through 1:83,000 the growth was as abundant as on the control. The next four tubes graded downward until the growth was scanty in a concentration of 1:41,000.

4. The *Microsporon audouini* grew to a concentration of 1:166,000. The growth was scanty at the 1:166,000 concentration, but was good on the tube preceding, (1:200,000).

As to the strength of gention violet necessary to inhibit the growth of the gram positive-bacteria, Churchmann [1] says: "Four gram-positive organisims were planted in broth tubes containing gentian violet in a dilution of 1:1,000,000, and at the same time control inoculations were made in plain broth. In none of the violet broth tubes did growth occur." "A dilution of 1:1,000,000 is thus seen to stop the growth of these organisms, and their growth may be retarded even by a dilution of 1:2,000,000."

We have repeated the above experiment of Churchman and obtained similar results. Grown on *solid* mediums, the dilution necessary to restrain growth of staphylococci was found to be between 1:500,000 and 1:1,000,000. The nature of mold work is such that solid mediums must be used, and our figures therefore will not run exactly parallel with Churchman's.

The concentration of gentian violet necessary to restrain the growth of the four molds above indicated was therefore found to be much stronger than that necessary to restrain the growth of gram-positive cocci and bacilli.

Technic of Second Experiment.—Following this preliminary work, which seemed to indicate in a general way that the mold group was more resistant to gentian-violet than the ordinary gram-positive cocci and bacilli, a series of fifty organisms including members of the mold group, the sporotricha and actinomyces, was planted on three concentrations of gentian-violet—1:500,000, 1:250,000, and 1:100,000.

The dilutions were made in Sabouraud's proof maltose agar from gentian-violet made by Grübler.

Results.—Cultures 1 to 28 inclusive grew on all three strengths of gentian-violet as readily as on the control with no apparent retarda-

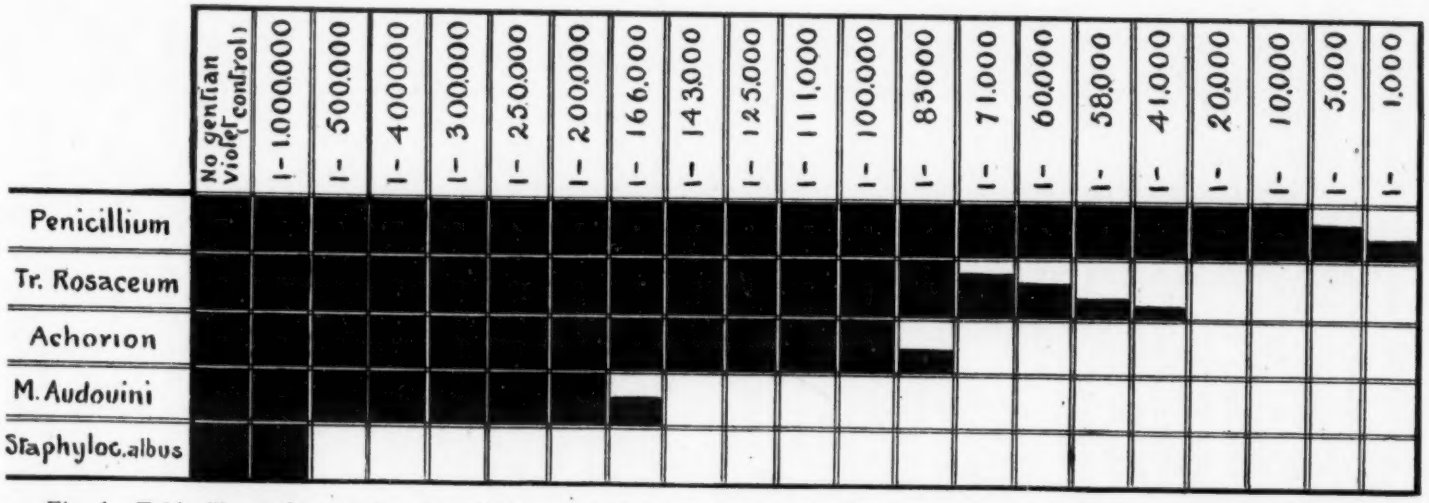

Fig. 1.—Table illustrating results of preliminary trials comparing growth of four molds with *Staphylococcus albus*, using gentian-violet at graded concentrations. The "stepped" effect is to indicate the abruptness with which luxuriance decreases as the restraining point is reached.

ORGANISMS USED AND SOURCES *

	D. R. No.	Source of Organism	Source
1.	(403)	Epidermophyton inguinale	U. P.—around anus
2.	(213)	Aspergillus variegatus	U. P.—nails
3.	(351)	Trichophyton gypseum	Paris—Sabouraud
4.	(253)	Trichophyton violaceum (?)	U. P.—scalp
5.	(407)	Microsporon lanosum	U. P.—scalp
6.	(336)	Achorion schönleinii	Paris—Sabouraud
7.	(358)	Penicillium brevicaule	U. P.—toe
8.	(219)	Epidermophyton inguinale	U. P.—thighs
9.	(342)	Trichophyton fumatum	Paris—Sabouraud
10.	(338)	Achorion gallinae	Paris—Sabouraud
11.	(341)	Trichophyton niveum radians	Paris—Sabouraud
12.	(344)	Trichophyton plicatile	Paris—Sabouraud
13.	(339)	Microsporon lanosum	Paris—Sabouraud
14.	(363)	Epidermophyton inguinale	U. P.—thighs
15.	(345)	Trichophyton rosaceum	Paris—Sabouraud
16.	(346)	Microsporon fulvum	Paris—Sabouraud
17.	(206)	Trichophyton album (?)	U. P.—favus scalp
18.	(201)	Trichophyton rosaceum	U. P.—leg
19.	(73)	Microsporon audouini	U. P.—scalp
20.	(86)	Trichophyton lanosum (?)	U. P.—cheek
21.	(316)	Epidermophyton inguinale	U. P.—thigh
22.	(364)	Epidermophyton inguinale	U. P.—thigh
23.	(295)	Microsporon audouini	U. P.—scalp
24.	(347)	Achorion quinckeanum	Paris—Sabouraud
25.	(212)	Microsporon lanosum	U. P.—scalp
26.	(298)	Epidermophyton inguinale	U. P.—thigh
27.	(350)	Epidermaphyton inguinale	Paris—Sabouraud
28.	(381)	Epidermophyton inguinale	U. P.—thigh
29.	(365)	Sporotrichum	K. F. M.—horse
30.	(366)	Sporotrichum	K. F. M.—dog
31.	(367)	Sporotrichum	K. F. M.—horse
32.	(368)	Sporotrichum	K. F. M.—man
33.	(369)	Sporotrichum	K. F. M.—animal
34.	(370)	Sporotrichum schenki-beurmanni	K. F. M.—horse
35.	(371)	Sporotrichum councilmani	K. F. M.—man
36.	(372)	Sporotrichum	K. F. M.—horse
37.	(373)	Sporotrichum	K. F. M.—man
38.	(374)	Sporotrichum	K. F. M.—horse
39.	(423)	Sterigmatocystis nigra	U. P.—nails
40.	(424)	Aspergillus aureus	U. P.—nails
41.	(425)	Aspergillus variegatus (T. Spec.)	U. P.—nails
42.	(426)	Aspergillus cyanicentris (T. Spec.)	U. P.—nails
43.	(427)	Penicillium nigra	U. P.—toe
44.	(428)	Keratophyton salmonica (T. Spec.)	U. P.—nail
45.	(222)	Achorion schönleinii	U. P.—favus scalp
46.	(420)	Microsporon lanosum	U. P.—scalp
48.	(422)	Achorion schöleinii	U. P.—favus scalp
49.	(430)	Keratophyton eburneum	U. P.—toe nails
50.	(1)	Actinomyces bovis	Philadelphia Veterinary School—Dr. Crocker
51.	(2)	Actinomyces bovis	Philadelphia Hygiene Lab.—Dr. Bergey

* U. P. indicates that the organism was isolated in this laboratory; K. F. M., from Dr. Karl F. Meyer, San Francisco.

tion. The sporotricha (29 to 38) inclusive grew readily on the concentration 1 : 500,000 and 1 : 250,000 without retardation and as luxuriantly as on the control. On the strongest concentration—1 : 100,000, however, there were differences. While *Sporotrichum councilmani* 35, grew as abundantly on this concentration as on the control and with no retardation, the remaining nine were retarded, the growth developing on an average four days later than the growth on the control. After growth began, the luxuriance was little if at all less than on the control except in the case of *Sporotrichum hamburger* 33, which grew scantily at all times even on the dilution 1 : 100,000.

Cultures 39 to 49 inclusive grew on all three dilutions as abundantly as on the control and with no retardation.

The two strains of actinomyces 50 and 51 were retarded in luxuriance of growth by even the weakest dilution of gentian-violet, 1 : 500,000. While there was a growth on this dilution, it was decidedly less abundant than on the control. There was no growth at all on the dilution 1 : 100,000.

Observations were made on all cultures over a period of four weeks.

COMMENT

All the organisms used had been isolated for some time from diseased tissue and were therefore thoroughly accustomed to growth on artificial mediums.

It is possible and probable that organisms growing directly from fresh material scrapings, etc., would have a different growth resistance to gentian-violet. The question of amount of material planted also arises in this connection; that is, a pure culture of an organism planted in fairly large quantity on artificial mediums, probably has a greater tenacity of growth than a small number of isolated organisms suddenly transplanted from freshly diseased material to artificial mediums. This question, however, can only be settled by the use of mediums in routine cultures over a notable time period. This we have already entered on.

We have used gentian-violet maltose mediums in the isolation of approximately twenty strains of pathogenic molds from fresh material, with no evident inhibition of growth of the specific organisms, and with apparently distinct advantage from the standpoint of restraint of contaminants. The concentrations used were 1 : 500,000 and 1 : 250,000 in Sabouraud's maltose mediums.

A difficulty yet to be overcome arises from the standpoint of the yeasts. Henrici [4] in his work on the straining of yeasts by Gram's method makes this statement: with the Gram stain "molds stain

4. Henrici, Arthur T.: J. Med. Res. **30**:409, 1914.

Fig. 2.—Fifty-one strains of higher organisms on three different concentrations of gentian-violet. Top row, gentian-violet 1: 100,000; next row, 1: 250,000; next row, 1: 500,000; bottom row control—no gentian-violet.

irregularly, isolated granules in the mycelia retaining the stain while large areas do not stain at all. The yeasts and bacteria are the only classes of cells in which this property (retention of Gram stain) is frequently found. . . . As far as I know all the yeasts are gram-positive."

Yeasts are frequently a contamination in cultures from the skin. We have not yet titrated the restraining power of gentian-violet on the wild yeasts, but in routine cultures of material for the pathogenic molds the wild yeasts do not seem to have been inhibited in the 1 : 500,000 strength of gentian-violet maltose agar.

It is evident that these gram-positive organisms (yeasts) are more resistant to gentian-violet than the ordinary gram-positive cocci and bacilli and in spite of their gram-positive qualities.

The two strains of actinomyces used, while growing on the weaker dilutions of gentian-violet, yet seemed to be less resistant to this substance than the ringworm group of molds, and to be in this respect more closely related to the sporotrichi. The small number of strains used, however, does not warrant sweeping conclusions.

SUMMARY AND CONCLUSIONS

1. A dilution of gentian-violet of 1 : 500,000 in solid (Sabouraud's proof) mediums will inhibit the growth of the gram-positive bacteria.

2. Fifty-one strains of the higher organisms were found to be capable of growth on maltose mediums containing gentian-violet in as high a concentration as 1 : 250,000. This group included epidermophytons, achorions, microsporons, trichophytons, sporotricha and actinomyces.

3. The organisms above mentioned, therefore, seem to be more resistant to the restraining action of gentian-violet than the ordinary gram positive bacteria.

4. We have used a gentian-violet maltose medium (1 : 250,000 and 1 : 500,000) in the isolation of approximately twenty strains of pathogenic molds with apparently good results.

THE CULTIVATION OF EPIDERMOPHYTON INGUINALE *

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In recent issues of *The Journal of Cutaneous Diseases* difficulties encountered in the cultivation of *Epidermophyton inguinale* have been discussed. During the past two years, in the routine culture of cases of epidermophyton infection in this clinic, we have encountered the same difficulties and have to some degree overcome them.

TECHNIC

Collection of Material.—In the collection of material, precautions should be taken to minimize as far as possible extraneous contamination, especially from the saprophytic molds, which are common inhabitants of the skin surface. The skin is cleansed with 95 per cent. alcohol and allowed to dry immediately before the scrapings are taken; the knife used in obtaining scales, and the black paper into which scrapings are received, should be sterile. A large amount of material should be collected.

Time of Planting.—Mitchell [1] has suggested that scales for cultivation be allowed to dry for several days before being cultivated, in order to eliminate some of the bacterial contaminants which do not resist drying as readily as does the epidermophyton. He states that he has succeeded in growing the organism after several months of drying in the laboratory. The recent work of Dold [2] on the viability of the epidermophyton indicates that some of the strains are not as resistant to the effect of drying as has been commonly supposed. Scales from four cases were filed at room temperature in sterile envelopes and were cultured by him at intervals. One case failed to grow on the twelfth day, three on the twentieth day, and all failed to grow after thirty days' drying at room temperature. Our own experience has shown that some strains are capable of resisting drying for long periods. In a series of cultures of old material we succeeded in one case in obtaining a growth of the organism from scrapings which had been filed in a dry paper envelope one year and two months previously

* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

1. Ormsby, O. S., and Mitchell, J. H.: Ringworm of Hands and Feet, J. A. M. A. **67**:711 (Sept. 2) 1916.

2. Dold, Herman: China M. J. **34**:34 (Jan.) 1920.

and in two other cases four months and five months before, respectively. However, we have also found that the epidermophyton both in cultures and in scrapings not infrequently appears to lose its ability to grow in a comparatively short time. This may be the effect of drying or some other unexplained agency, but we feel that more cultures of the organism are positive when the material is planted soon after collection.

Culture Mediums and Plates.—A plate method that obviates the drying out of medium over the long periods of time necessary for mold culture, gives easy accessibility to the medium surface for plant-

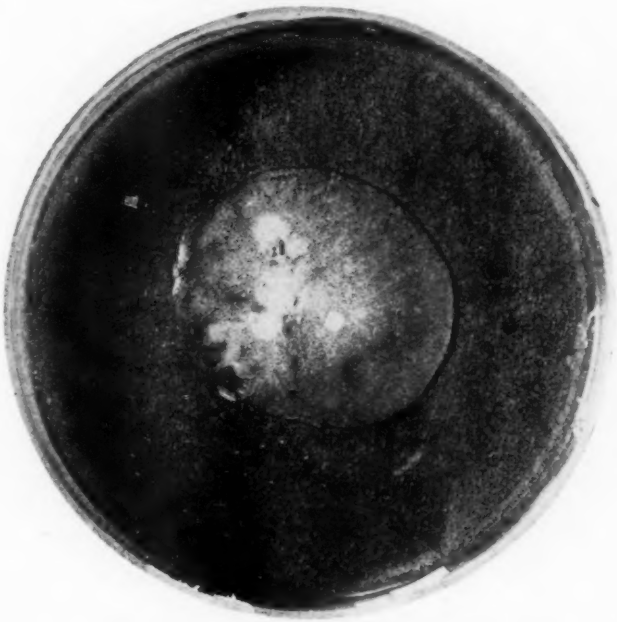

Fig. 1.—Top of culture, looking through the glass plate which serves as a cover.

ing and picking colonies and at the same time lowers chances of contamination, has been found to be more or less satisfactory and may be worthy of description in detail. Melted agar medium cooled to 45 C. is allowed to run slowly from a pipet into a Petri dish so that an area of hardened medium is formed in the center of the dish leaving a zone free of medium about it. This prevents secondary contamination from creeping in from the edges as so often happens when the entire area of the floor of the Petri dish is filled with medium.

As soon as the agar is well hardened the dish is inverted, the lid removed, and the half containing the medium carefully placed on a sterile glass plate 8 by 6 inches (reclaimed photo plate). Melted paraffin is then painted around the contact circle of the plate and Petri dish with a small brush thus sealing the chamber. Before planting, these modified Petri dishes are allowed to incubate at room temperature for a few days to insure their sterility, a stock being kept on hand.

Three varieties of medium have proved useful in the culture of the epidermophyton, and as a rule one plate of each variety of medium is seeded in each case.

Fig. 2.—Bottom of culture. One half of the Petri dish is attached to the glass plate with paraffin.

SABOURAUD'S PROOF AGAR: This medium is made according to Sabouraud's [3] recipe. It may be worth while to call attention to the fact that most English textbooks on bacteriological technic, while specifying the amount of maltose correctly, fail to specify that the maltose must be commercial maltose and not the chemically pure product. Professor Sabouraud is emphatic in calling attention to the sparsity of growth on the chemically pure sugar medium. "Toutes les maltoses, soi-disant pures, que j'ai essayées, donnent des cultures, d'une médiocrite insigne, alors que la maltose commerciale dont je

3. Sabouraud: Les Teignes, 1910, Paris, Masson et Cie, p. 111.

me sers donne des cultures admirablement belles et differenciées." (All the so-called pure maltoses which I have tried give cultures of a mediocre character, while the commercial maltose which I use gives cultures, very beautiful and distinctive.)

BLOOD SABOURAUD'S MEDIUM: Human blood which has been heated to 55 C. for thirty minutes is added to Sabouraud proof agar in the proportion of from 3 per cent. to 5 per cent. and plates made as described. This medium has given us positive cultures when the first plate failed to show the organism, and we feel that it is of advantage.

GENTIAN-VIOLET BLOOD MALTOSE AGAR: Churchman's[4] work on gentian-violet has shown that this substance possesses the peculiar property of inhibiting the growth of gram-positive organisms in high dilutions. In a preceding paper we have published the results of preliminary experiments on the effect of gentian-violet on four members of the mold group of widely varying cultural characteristics, which seemed to indicate that gentian-violet exhibited its restraining effect in much higher dilution on gram-positive organisms than on the mold group. We have applied this in the culture of epidermophyton, which is apparently not at all inhibited in the dilution of 1:500,000, which is sufficient to inhibit the gram-positive organism.

In practice a 1:100 watery solution of gentian-violet (Grübler) is kept as stock. A 1:10,000 dilution is made by adding 0.1 c.c. of the stock to 9.9 c.c. of distilled water, 0.2 c.c. of this dilution is added to 10 c.c. of Sabouraud's proof agar, making a final dilution of 1:500,000. Blood is added to this medium in the proportion outlined and the medium plated. The agar should be free of phosphatic sediment as the sediment takes up relatively large amounts of the dye and thus interferes with the proper dilution.

SEEDINGS: A large amount of the scrapings is planted on each plate. This is an important point.[5]

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4. Churchman, J.: J. Infect. Dis., 1912.

5. In addition to the references already given, the following may be of interest:

White, C. J.: J. Cutan. Dis. **37**:501 (Aug.) 1919.

A NOTE ON THE DISSEMINATION OF SPIROCHAETA PALLIDA FROM THE PRIMARY FOCUS OF INFECTION*

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Although it is now generally recognized that the time during which a syphilitic infection remains confined to the primary focus of entry is comparatively short, and that the effort to distinguish between a localized and generalized stage of infection is largely an arbitrary one, no one has shown just how rapidly the infecting organisms may spread after they have once gained entrance to the body or when a generalized infection may be said to have occurred. These are questions of obvious clinical importance and considerable light may be thrown on them by the sequence of events which follows local inoculations of *Spirochaeta pallida* in the rabbit.

In a recent series of experiments, an attempt was made to obtain some data on these points by a systematic determination of the presence of spirochetes in the inguinal lymph nodes and the circulating blood of rabbits at various intervals after scrotal or testicular inoculation.

The organisms used in these experiments were old strains, one of which was isolated by Nichols and Hough in 1912 and the other by Zinsser and Hopkins in 1913. They have been maintained in rabbits for periods of nearly seven and eight years.

TIME OF INVASION OF THE REGIONAL LYMPH NODES

The method used for determining invasion of the regional lymphatics was the excision of the inguinal nodes (under ether anesthesia) of rabbits that had been inoculated by the introduction of a small bit of infected tissue beneath the skin of the scrotum and the injection of an emulsion of these nodes into the testicles of normal rabbits. In all, inguinal nodes from twenty-nine rabbits were examined by this method.

The first series of examinations was made on rabbits showing definite primary lesions and well marked lymphadenitis in order to test the method on cases in which infection and involvement of the regional lymphatics were both apparent. The period covered by this

* From the Laboratories of the Rockefeller Institute for Medical Research, New York.

series of examinations was from sixteen to sixty-one days after inoculation, and spirochetes were demonstrated in the nodes of all these animals.

With this data available, the time between inoculation and excision of the nodes was then progressively reduced to seven, five and two days. These periods were again fixed with reference to pathologic changes. The five and seven day periods corresponded roughly with the time at which definite enlargement and induration of the inguinal nodes could nearly always be recognized, but usually antedated the appearance of the initial lesion, while little or no alteration could be detected in the nodes within the first forty-eight hours.

There were twenty-three animals in this group. In two cases (seven days), spirochetes were demonstrated in the nodes by dark field examination and no inoculations were made from this material. The other nodes all gave positive results by animal inoculation, thus showing that extension of the infection to the inguinal lymph nodes antedated both the appearance of the initial lesion and the occurrence of definite alterations in the nodes themselves, and that this occurred constantly within a period of less than forty-eight hours from the time of inoculation.

INVASION OF THE BLOOD STREAM

Supplementing the observations on invasion of the lymphatics, a series of experiments was carried out to determine the time and frequency of blood stream invasion. The mode of determining the presence of *Spirochaeta pallida* in the blood was by bleeding from the heart, defibrinating and injecting 0.5 c.c. of blood into the testicles of normal rabbits.

In the course of these experiments, a large number of bleedings was made covering the time from the appearance of the initial lesion (twelve to fourteen days after inoculation) through various periods of its development, with the result that spirochetes were shown to be constantly present in the circulating blood by the time an infection could be recognized at the point of inoculation.

A small series of animals was then bled arbitrarily at an interval of one week after inoculation and it was found that even as early as this spirochetes were sufficiently numerous in the circulating blood to produce infection when amounts as small as 0.5 c.c. were injected into the testicles of normal rabbits.

THE ESTABLISHMENT OF A GENERALIZED INFECTION

In view of the results obtained from examinations of both the inguinal lymph nodes and the circulating blood of infected animals, there seemed to be no real object in attempting to determine more

exactly the time at which spirochetes could be recovered from either the lymphatics or the blood stream. However, there might be some legitimate question as to whether a dissemination of spirochetes, such as had been shown, could be regarded as a true generalized infection. In order to settle this point, ten rabbits were inoculated in the right scrotum only and forty-eight hours later the entire scrotum and testicle of this side were amputated under ether anesthesia. In spite of the complete removal of a wide zone of tissue surrounding the area of inoculation, all of these animals developed syphilitic lesions, thus showing that true infection of parts outside of the zone of operation had taken place within the brief period of forty-eight hours.

CONCLUSIONS

While the conditions of these experiments are not entirely analogous to those that obtain in cases of human infection, the general course of events is undoubtedly much the same in the two cases.

It would appear, therefore, that, for practical purposes, there is probably no appreciable time during which a syphilitic infection can be regarded as confined to the focus of entry but that, immediately infection takes place, the spirochetes begin to multiply and invade the surrounding tissues, gaining access to both the lymphatics and the blood stream, and are widely distributed over the body even before an initial lesion can be detected.

The early appearance of a distinctive lesion at the site of infection and the lapse of time required for the development of generalized lesions are to be viewed more as a result of a sequence in localization and concentration of spirochetes at given points than as indications of the time required for their dissemination.

THE CLINICAL APPROACH TO SYPHILIS, WITH SUGGESTIONS FOR ITS REVIVAL AND DEVELOPMENT *

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For the past four years, a large part of my time has been occupied with the development of clinical interest in syphilis in the diagnostic group of the Mayo Clinic, through whose hands pass approximately 60,000 patients a year. In developing a diagnostic and therapeutic approach to the disease I have been compelled to give constant and intense thought to the present and future possibilities, limitations, and tendencies of syphilology as a special field of medical activity. As a dermatologist, I may be pardoned for bringing before you for your criticism and suggestions some of my impressions and perplexities. I have passed through a period of misgivings and distrust of the possibilities of the work, engendered in part by the confusion and lack of cooperation which at first sight appears to pervade the field, and in part by the feeling that the clinical syphilographer as such reached his culmination in Fournier and that others who in these times essay the rôle can be no more than base imitators. In the grip of that depression I cast yearning eyes on the laboratory, as many a better man has done, and longed for the day when with a corps of trained routinists to buttress me against the demands of patients, I could indulge in a species of endowed reflection in sequestration, and in animal experiment. From this monastic phase I am slowly emerging in response to a new appreciation of the enduring worth and ultimacy of clinical research.

The critical problem of the next half century of syphilology, as it has appealed to me during the past several years, is not so much the extension of the laboratory knowledge now so highly developed, as the application of the knowledge already existent, to the pressing clinical problems of the disease. No reasonable man would seek to minimize the worth of the laboratory contribution, whose fundamental character needs no discussion in this assembly. But a decade of transformations has been superimposed on the clinical syphilology of Fournier, Hutchinson and Morrow as two fluids of different densities may be superimposed the one on the other in a test tube. I believe that there has never been a greater need for clinical revision of laboratory specialization in the diagnosis and treatment of syphilis. The Was-

* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

sermann reaction is passing from the phase of uncritical acceptance to one of almost reactionary distrust. Adequate examination of the spinal fluid has transformed our conceptions of neurosyphilis, and the postmortem identification of the *Spirochaeta pallida* in the tissues of treated and supposedly cured syphilitics has compelled a much needed return to conservatism in our therapeutic enthusiasm based on modern chemotherapy. In helping to make the clinical readjustments for which the need is so pressing, it seems to me that man may yet aspire to the laurels of a Fournier. The field of clinical syphilology, instead of being closed, has just been thrown open anew.

My struggles to become in more than name the syphilographer of the Mayo Clinic, epitomize, I believe, something of the course which clinical syphilology must run in the next few decades, much as the ontogeny repeats the phylogeny in von Baer's law. Coming to my work primarily as a dermatosyphilographer, I found myself confronted point blank with phases of the disease with which my acquaintance was of the remotest. To witness the completeness with which syphilis of the stomach had been worked out by the men whose colleague I became, to learn of diagnostic signs such as neurogenous bladder whose existence I had never suspected, was an experience calculated to remove every trace of the bumptious from my conceptions of my position. Consciously or unconsciously the diagnostic group of the Clinic taught me syphilology in at least as full a measure as I taught them. They have taught me so effectually that I am all but a convert to the belief that the future of modern syphilology is in the hands of the group and that the day of the syphilographer who can combine in his sole personality both the technical attainments and the wealth of general and detail knowledge that make him a master of the disease, is past.

Appreciation of the complexity of the procedures, on which the modern intensive study of clinical syphilis depends, grows on one as his experience with group practice develops. For my own information I recently summarized the list of examinations on which at one time or another my department relies for a diagnosis or information on the status of a syphilitic infection (Table 1). This complex instrument involves the most extraordinary range and combination of structural and functional tests imaginable. As one's facilities for employing it extend and one's acquaintance with the instrument develops, he appreciates more and more how illusory is the hope that syphilis will ever yield to a single diagnostic key. Yet it is precisely this search for a touchstone in syphilis as in other diseases, which in this day betrays the large body of medical practitioners into an unthinking, if temporary, worship of single procedures such as the Wassermann reaction and the luetin test.

TABLE 1.—The Multiple Procedure Diagnostic Attack on Syphilis

1. Intensive study of the anamnesis
2. Social estimation of the case
3. Study of the family both in history and examination
4. Serum Wassermann reaction (single antigen)
5. Modifications and intensifications of the serum Wassermann test, such as the provocative, cold fixations, multiple antigens and Wassermann series
6. Examination of the cerebrospinal fluid (two Wassermann tests, Nonne, cell count on the fresh fluid, colloidal gold test)
7. Darkfield examination and stains of fresh secretions
8. Luetin test
9. Levaditi and other tissue stains
10. Neurologic examination
11. Eye examination
12. Ear examination
13. Nose and throat examination
14. Dermatologic examination of the skin and mucous membranes
15. Visceropathic studies of the liver and spleen, and of the stomach, involving the study of anemias, blood dyscrasias, test meals, esophagoscopy, roentgen examinations and so forth
16. Special cardiovascular examination, including the physical findings, blood pressure, electrocardiographic examination, and so forth
17. Roentgenologic examination
18. Exploratory operative procedures (seldom used until after the therapeutic test)
19. Genito-urinary examination
20. Therapeutic test
21. Necropsy

The rapid modification of the clinical knowledge under the pressure of new technical diagnostic and therapeutic methods has induced a peculiar state of disorganization in the syphilologic realm. True syphilology is for the time being lost in the mazes of an analytic era and the syphilologic workshop is crowded with personalities each so intent on the part which he contributes that he can give no thought to the whole. It comes about, therefore, that in the search for a syphilologist one encounters instead of the single master an astounding procession of partial personalities and hyphenates: the interno-syphilographer, the sero-, the neuro-, the dermato-, the gyneco-syphilographer, the syphilo-therapist and syphilo-pathologist, even the ophthalmo- and oto-syphilographer, and last, though far from least, the genito-urinary or penile syphilographer. The syphilologist of the future is as yet in a phase of mental dissociation suggesting the unfortunate condition of the Miss Beauchamp of Morton Prince's [1] study. Unless some means can be found to synthesize a single personality from the existing parts, Fournier will indeed have been the last of the great masters.

1. Prince, M.: The Dissociation of Personality, New York, Longmans, 1906.

The problem of today, then, in syphilology is to introduce a synthesist among the analysts, and to provide the workshop of syphilology with an assembler as well as with makers of parts. My experience, such as it is, has all but convinced me that in the development of coordinators rather than performers of new technical tests lies the really great opportunity in this field of medicine.

THE IDEAL SYPHILOGRAPHER AND SYPHILOLOGIC SERVICE

I confess that I do not see how it is possible for one man to unite within himself both the powers of synthetic interpretation and of detailed technical performance which modern syphilology requires. In his effort to become a syphilographer, therefore, our future Fournier must in a measure, it seems to me, choose between technical proficiency and intellectual grasp of principles. Ability to perform an irreproachable Wassermann test, to examine the fundus of the eye, to carry out a complete neurologic examination or to cystoscope a bladder may be graces of accomplishment, but I believe that they subside into secondary importance in comparison with the vital need for a tremendous breadth of outlook on the disease. By his coordinating power, by his just appreciation of the worth of each single test and manifestation, and yet of the immeasurably greater possibilities of the interpreted whole, the syphilographer of the future will stand or fall. He will be that type of clinician whose success will be measured to no small degree by ability to secure the hearty good will and cooperation of colleagues. Having secured it, he must be able to focus to a point their individual proficiencies in special procedures, which if they were employed alone or in discordant competition would defeat the issue.

The search for a syphilographer, and the training of one, becomes, therefore, essentially the finding and development of a certain type of man. It is unquestionably desirable that he should have exhaustive training in one or more of the special contacts which syphilis makes in medicine. He must at least also have speaking acquaintance with all the elements of his work, or he will be a narrow expounder and a poor cooperator. The point I want to emphasize, however, is that it is personality and breadth of viewpoint, not the dermatologic or the urologic or the internomedical training, that make a syphilographer. Nothing so becomes a true syphilographer, it seems to me in these days, as humility and the willingness to seek aid from experts whose acquaintance with the borderline of syphilis within their special fields may perhaps be greater than his own.

Many of you, I fear, will accuse me of reducing the syphilographer of the future to a hopeless parasitism on associates. Such a parasitism might perhaps develop were the syphilographer to confine himself merely to a judicial interpretation of the work of colleagues. In order

to keep himself fresh and to retain that enthusiastic interest in the disease which is the first essential to the inspiring of others, the true syphilographer must have and preserve his forte or specialty as he extends his experience. Happy is that syphilographer whose forte encourages objectivity, keenness of observation and the ability to weigh dispassionately and decide quickly. For these four qualities, which have so much in common with the essentials of success in every life activity, no technical proficiency in examination or manipulation can ever serve as substitute.

It is because I have believed that the dermatologic training at its best develops and fosters these qualities, that I have always been partial to the dermatologic forte for the syphilograhper. It is also because I have come to realize how impossible it is for any one special group in medicine to annex syphilology as a perquisite that I have mentioned in an emphatic way how much the Mayo Clinic itself contributes to my personal development along syphilologic lines. I am filled with enthusiasm for the amount of syphilology that can be learned and taught in the course of modern routine medical and surgical diagnosis. You will, I am sure, pardon my perhaps over-ardent advocacy of the group diagnostic attack on syphilis. I cannot but contrast with it my own situation as an isolated unit, when in the effort to live up to the responsibilities of a syphilographer I, in company with the other hyphenates and partial personalities, wielded fragments of the potential syphilodiagnostic and therapeutic machine as if all other parts were nonexistent. Such an experience makes one sympathetic with the problem of the general practitioner in the diagnosis of syphilis, as he gropes with his Wassermann lantern through the dense forest of spirochetal possibilities.

Appreciation of the problems I have brought up has a practical bearing on the way in which one attempts to develop the clinical approach to syphilis among his confrères. To this problem there are many aspects beside the principle of exclusive title to the treatment of all patients with syphilis, about which the controversy usually seems to rage. Personally I believe that the ideal syphilologic service is not created by any fiat of hospital or medical school authorities but by the personality which is essential in the makeup of the syphilographer. The man whose conception of syphilologic progress consists of personal aggrandizement will probably make himself lasting enemies by his efforts to absorb the serology, the roentgenology, and the various other special aspects of the diagnosis of the disease. A much more ideal condition is created, it seems to me, when the would-be syphilographer, whatever his forte, gains his following by the spontaneous recognition on the part of his confrères of his enthusiasm and his special equipment for his post.

It will be apparent from what I have said of the syphilographer of the future, that organizing duties will form no small part of the field for the exercise of his energies, and that a recognition by the partial syphilographer of today of the salient responsibilities which his successors will inherit, will do much to lighten their task of creating a new clinical syphilology. Five major duties rest on those of us who raise the cry in the wilderness, "Prepare ye the way".

DUTIES TO BE PERFORMED IN CREATING A NEW CLINICAL SYPHILOLOGY

The first duty is to lift syphilis, the object of our interest, from the field of routinism. Routine interest, or perhaps routine lack of interest, is the curse of all large medical organizations. Some of the poorest syphilologic diagnosis in the world is, to my mind, the product of the routine Wassermann test on patients entering hospitals. Even though the quantitative yield of recognized syphilis be large by such a procedure, and even though it may be an ultimate desideratum to inaugurate a modified routine system, it deserves only secondary, and not the primary emphasis usually accorded it. Routine procedures discourage the alert suspiciousness of mind and zest in ferreting out the disease that is a fundamental attribute of the true syphilographer, and which he must develop to the highest possible degree in his clinical cooperators.

Ferretting being so large a part of the work of the syphilodiagnostician, his second duty is to inspire associate ferrets, so to speak, in the form of fellow clinicians, who can be specially interested in particular aspects of the general problem. Nearly every medical examiner in a group can hear a heart murmur. Usually only one in a group cares to develop to its utmost detail the art of recognizing the earliest manifestations of cardiovascular syphilis. To have the personal gift and the ability to present the problem of syphilis to a colleague so as to inspire him to contribute his diagnostic acumen to the study of some particular aspect of the disease is one of the hall marks of a successful developer of the new clinical syphilology.

The third duty of a syphilographer as I conceive it, and one well calculated to compel a judicial frame of mind and a wide acquaintance with the disease, is that of developing means of checking the results of individual diagnostic, therapeutic, and research procedures against each other and against the general knowledge of the disease which develops as a result of such experience. The syphilologic service thus becomes a clearing-house for information and opinion and a court of last resort in diagnostic decision. As its presiding officer, the syphilographer is under obligation to formulate the experience of the court at frequent intervals, in as concise and conclusive terms as possible. With this end in view my own department, in addition to its

formal publications, issues at frequent intervals, a house letter, which aims to epitomize current progress in the field covered by the Section of Dermatology and Syphilology.

Duty number four of the syphilologic pentalogue is to make impressionism and intuitive diagnosis take tangible form and exact expression so far as possible. Diagnostic instinct in particular, so often summarized in the slang term "hunch," only too often perishes with its possessor, leaving the next generation to develop it anew. Medicine in general, and diagnostic syphilology in particular, possesses all too few of those landmarks of synthetic thinking in the form of exact, almost mathematical expressions of great principles, which adorn the more exact sciences, such as organic chemistry and physics, and which are familiar in bionomics and actuarial science. This problem of developing a mathematical and statistical syphilology is intimately connected with the last item of the pentalogue.

The mastery of data, the fifth duty, is one of the most practical and at the same time, I believe, one of the most pressing of the obligations of those who are preparing the approach to a new clinical comprehension of syphilis. The matter of records is a live one in every field of medicine. Not more than a month ago I received a letter indicating that general attention is already beginning to focus on this question in connection with the venereal diseases. On an adequate system of record quite as much as on acuity of observation, we must depend for the great body of facts and the means of detecting their interrelations which seem so conspicuously lacking in the disorganized syphilology of the present day.

There is no better exercise in humility than after four years of effort terminating in the formulation of a policy such as this, to look back on the undone in the light of one's accomplishment. To this wholesome discipline I have endeavored to subject myself during the past six months in an extended search of the records of my department for evidence of the success or failure of my policies. That I had only half envisaged the problem, in at least one of its aspects, became apparent when I was forced to discard outright nearly a thousand of the records collected during the first two years of my work. Each new effort to meet the situation has, however, brought to light new suggestions and experience to apply toward the development of the program. I would like to present briefly some of the ideas developed by such a review.

THE PERSONAL EQUATION IN INTERPRETATION OF CLINICIAN

No individual clinician is living up to the obligations of his work who is not questioning himself searchingly from time to time as to the personal equation factor in his interpretation and the consistency

and logical development of his thought. The same obligation rests on one who endeavors to focus through his department the diagnostic and investigative work in syphilis carried on by his team mates. Consciousness of this obligation has been at the background of my own repeated insistence on the need for personal acquaintance with the serologist and the serologic technic underlying the Wassermann test which one employs. In these days of Wassermann enthusiasm it takes considerable courage to face a group of clinicians with the assertion that a positive Wassermann reaction is false because absolutely nothing else can be found to substantiate it. Such assertions about the negative Wassermann reaction have of course become commonplace. It is a pleasure to see in recent publications a growing tendency to recognize that the positive reaction has an appreciable margin of error which increases in direct proportion to the sensitiveness of the technic. Even the serologist is not free from subjective interpretation and is prone at times to assume title to a degree of clinical judgment which he does not possess.

Subjective interpretations and hence personal equation constantly enter into the decisions of every type of clinician regarding the advisability of making a special investigation for syphilis. Not a few of these interpretations rest on the syphilology of the past generation and the worse than incomplete teachings of even the good medical schools. Each of us unconsciously carries in his mind a few syphilologic *ipse dixits* such as "pupillary irregularities mean syphilis" and "lowered bone conduction is pathognomonic," "interstitial keratitis always involves the other eye," or "ununited fractures have no relation to syphilis." The syphilis in these rules of thumb is often the old time syphilis recognized only when there is a history of every visible accompaniment of the infection, or it is the Wassermann bound syphilis of the last ten years. It is too easy in these days to forget or not to know that there may be syphilis apparent to a neurologist which a rhinologist may never recognize and which consequently never enters into his calculations. There is also, conversely, a catch-basket syphilis which like "rheumatism" serves as a convenient place for the obscure and puzzling manifestation, whether or not due to syphilis. In both cases a partial outlook on the disease leads to erroneous generalizations, which, when announced *ex cathedra* by a clinician with a positive manner, create diagnostic flurries that require much laborious effort on the part of a true syphilographer to evaluate and perhaps correct. One of the most famous or perhaps better, infamous of *ipse dixits* of the type I mean, was the endorsement of sodium cacodylate by an otherwise brilliant surgeon, a piece of unqualified impressionism which has done untold harm and will require even greater labor than Cole [2]

2. Cole, H. N.: A Study of Sodium Cacodylate in the Treatment of Syphilis, J. A. M. A. **67**:2012, 1916.

has expended on it, to correct. The evaluation of subjective interpretations and the struggle against a tendency to clinical dogmatism, both in himself and his confrères, must absorb a considerable portion of the energy of a true syphilographer.

I have already suggested the importance of lifting syphilis from the dead level of routine consideration or lack of it. This is what I call raising the index of suspiciousness in oneself and in one's diagnostic group. A definite pitfall awaits the worker on this phase of the problem. There is unquestionably a hypersuspiciousness, well illustrated by a case which I saw at one time with Dr. Pusey. A young man with a herpes progenitalis had sustained Wassermann tests and darkfield examinations, *ad lib.*, two spinal punctures, a circumcision and a biopsy on the glans penis, in the effort to make a syphilitic out of him. By the time this unfortunate victim of hypersuspiciousness reached the care of the distinguished conservative who finally set him right, he was in a mental state beyond description. On the remains of his glans penis he bore a recurrence of as obvious a herpes progenitalis as a dermatologist could imagine. The inevitable subjectivity of even our most important intuitive diagnosis, the recognition of the facies of hereditary syphilis, has also its amusing side. My associate brings to me an only child asking me to pass on the boy's appearance. I fail to get the intuitive impression, and so express myself. My associate then requests the boy to open his mouth and demonstrates to me the cicatricial deformity of the nasopharynx so frequently seen in association with late syphilis. The boy closes his mouth and stands before me transformed in appearance by my subjective inner mind. I seem to see his face studded with the stigmas whose existence I repudiated but a moment before. Subjectivism and impressionism can creep unconsciously into the most unsuspected angles of the most cold blooded statistical research. In my mention of records I shall point out how essential it is, therefore, to secure automatically and without prejudice certain data that satisfy the requirements of scientific control. I[3] published during the past year a deliberate check on an impression with regard to syphilis in railroad men. The statistical investigation, which was carried out on cases about which there had been no presuppositions, seemed to demonstrate a peculiar prevalence of neurosyphilis in this social group. Knowing the intense nervous strain to which most of them are subject I embraced with enthusiasm the seeming etiologic relationship and indulged in rash, though fortunately not published, expressions on the occupational factor in the course of syphilis. A subsequent investigation of farmers, now in progress, has abruptly checked my enthusiasm. Preliminary indications are that neuro-

3. Stokes, J. H., and Brehmer, Helen E.: Syphilis in Railroad Employees (A Clinical Study of an Occupational Group), J. Indust. Hyg. **1**:419, 1920.

syphilis will be as prevalent in this wholly different occupational type as among railroad men. Is it then a neurotropic civilization or a neurotropic spirochete that underlies the situation, or will my etiologic dream evaporate into the commonplace explanation that neurosyphilis is the least familiar aspect of the disease to the general practitioner, and for that reason the one most likely to reach a syphilographer associated with a last resort diagnostic clinic? Conjugal neurosyphilis, another example of pseudo rarity due to impressionism, in its day stood out "like a lighthouse," to use Pusey's[4] effective phrase. I suspect that it will subside into a commonplace under the diagnostic attack of the new syphilology, which has so many ways of demonstrating early neurosyphilis, that the person with syphilis, whether husband or wife, who escapes the demonstration of some involvement of the nervous tissues, will be the exception rather than the rule. May I align one more aspect of impressionism with those that have gone before? I refer to impressionism in syphilotherapy, with special reference to the fact of cure. In preparation for a hearing before a congressional committee, in which I expected to be examined on the minimum of treatment necessary for cure, and in which I had prepared the usual anathema for mouth medication and the usual panegyric in favor of arsphenamin, the spirit moved me to check up my stock phrases with a little study of my own records. The study was an abortive one, rendered abortive, not by lack of interesting findings, but by the glaring defects of the ordinary system of record. We carried it far enough, however, to make us realize that some patients attained clinical cure on so little and some others go on to the gravest complications on so much, that the last thing a true syphilographer would dare to do would be to dogmatize on therapy and cure.

OBJECTIVE INTERPRETATION OF THE DISEASE

The obvious remedy for situations such as I have described lies in recourse to the objective as distinguished from the subjective interpretations of the disease. Syphilis is a disease with a low subjectivity and a high objectivity. Yet in this field also one encounters the gravest of problems. Objective tests for syphilis consist essentially of examinations for structural and for functional changes, the one type naturally merging itself at times in the other. The standard of reference for the structural tests must be the visible norm determined by experience. Visible conceptions of the normal are the easiest to obtain and, like all visual impressions, have a satisfying degree of concrete-

4. Pusey, W. A.: Syphilis as a Modern Problem, Chicago, American Medical Association, 1915.

ness. It is precisely the possession of visible interpretative norms which gives the dermatologist and ophthalmologist their opportunities for syphilologic diagnostic éclat. Just as most people have visual memories and visual standards of judgment, so the visual norm in syphilologic diagnosis is the safest, and tests in which something can be seen are among the major assets of the syphilographer.

Nonspecificity in tests for structural change places a distinct qualification on their value. The weaknesses of such tests are apparent in the physical diagnosis of abdominal lesions, and in the roentgenologic picture of syphilis of the lung, and at times in that of certain bone changes such as periostitis, in which there seems to be doubt as to whether a true syphilitic picture exists. The electrocardiographic study of the condition of the myocardium thus far at our hands has yielded largely nonspecific results. The evaluation of the degree of nonspecificity in a test for syphilis can only be accomplished by a search for collateral evidence and it is precisely in this direction that the true syphilographer should be of the greatest service.

The functional test for syphilis is rendered more uncertain and confusing in interpretation by the difficulty of establishing a definite norm in the absence of visible changes. A definite norm and standardized conditions of performance are just as essential parts of the interpretation of syphilologic functional tests as they are of structural tests. We have had opportunity to appreciate the confusion which a lack of functional norms may introduce into the interpretation of tests for syphilis in our study of bone conduction in the diagnosis of the disease, in the interpretation of the Bárány tests for inflammatory changes in the brain stem, and in our comparison of records of various observers on the behavior of the pupil. In our work on bone conduction,[5] for example, it was found that under standardized conditions reductions up to four seconds, formerly accepted by some clinicians as almost pathognomonic of syphilis, are within the normal range of variation of the test, and that complete analysis of the results placed still further qualifications on its diagnostic value. The importance of standard conditions for the performance of pupillary reaction tests becomes apparent when the complexity of the mechanism and the factors influencing the response is considered. The neurologic examination itself is a conspicuous example of multiple functional tests for structural abnormality. It derives its value from the fact that the individual parts of the multiple procedure serve as checks on each other. There could be few better patterns after which to model the syphilologic diagnostic machine than the complete neurologic examination.

5. Goeckerman, W. H.; Barlow, R. A., and Stokes, J. H.: The Diagnostic Value of Lowered Bone Conduction in Syphilis, Am. J. Syph. **3**:240, 1919.

GROUP WORK AND MULTIPLE PROCEDURE IN SYPHILOLOGY

After such an elaborate analysis of the problem of syphilologic diagnosis and clinical interpretation I may be pardoned if I raise one more question. Is the value of individual experience with the disease as a whole lost by group methods of investigation, and does the scattering of the problem through a number of personalities multiply the subjectivity and personal equation factors to the point where the results become unreliable? An incidental type of answer to this question appeared in the course of the study of syphilis in railroad men already referred to. The original statistical analysis was based on a group of fifty cases taken at random from the files. In offering the study for publication I was rebuked by an editor for presenting conclusions based on insufficient data. In order to vindicate my confidence in the ability of the diagnostic group to paint with accuracy the clinical picture of syphilis from a comparatively small number of cases, I compared with the first group a second group of fifty unselected cases taken from the files (Table 2). The parallelism of the results appears to me to be a vindication and an index of the accuracy and consistent quality of group work in syphilology. It seems after all not unreasonable that the increased exactitude of tests performed by specially trained men will more than compensate for some increase in subjectivity, and that the checking of the personal equation of one against that of the other will greatly reduce rather than increase the ultimate importance of this factor.

Multiple procedure in the examination of syphilis makes life anything but easy for the syphilographer, whose lot it is to carry his work through the complex interpretations that underlie diagnostic and therapeutic decisions. Subconscious reasoning and temperamental factors inevitably enter into the work of synthesis. Given a childless young married woman with a positive Bárány finding, indicating a diffuse lesion in the brain stem, a single ++ Wassermann reaction in a provocative series of seven tests, a bone conduction of — six seconds, and negative spinal fluid, a history of a father who died abruptly of heart failure and relief of dizziness on therapeutic test with a subsequent relapse under inunctions. What is to guide me, in the absence of facies and stigmas, to a diagnosis of obscure heredosyphilis? In one mood my intuitive sense that something ought to underlie such a complex might lead me to ask for an examination of the patient's mother and sister, to find confirmed in them my suspicions as to the nature of the process in the original patient. On another occasion a correct solution might wholly escape me. On still a third occasion a fortuitous necropsy might send my card house of suspicions tumbling about my ears. To decide just which of a complicated group of findings deserves major consideration, just how much weight each

TABLE 2.—Comparison of Duplicate Surveys of Two Groups of Fifty Railroad Men Each *

	Percentage	
	First Series	Second Series
Cerebrospinal fluid positive	64	79
Lues, central nervous system	79.5	83
Lues III, cardiovascular	18.7.	20
Blood Wassermann negative	57	58
Blood Wassermann positive	43	42
Wassermann weak positive	4	2
Use of alcohol	75	61
Heavy drinkers	36	33
History of lues II unobtainable	62.5	60
Lues recognized at some time	55	57
Age of onset of late symptoms—over 30	78	75
Gonorrheal history positive	80	73
Gonorrhea only	24	19
Symptoms appearing from six to twenty years after infection	71	67
Per cent. infected by the age of 32	91	81
Wassermann on men under 25 will reach	70	60
Sterile or pathologic marriages	44	50
Age on entry—patients between 25 and 40	32	36
Concerned in operation of trains	76	70
Concerned in operation of engines	36	36
SYMPTOMATOLOGY		
Gastric	28	22
Not suggestive of lues	18	24
Headaches and head pains	16	16
Cardiac	14	16
Diplopia and poor vision	14	10
Malaise, weakness	12	8
Shooting pains	10	20
Bladder (subjective)	10	4
Nervousness	8	4
"Do I have syphilis?"	8	6
Laryngeal	8	6
Rheumatism	4	18
Ataxia (subjective)	4	6
Girdle pain	4	4
Dizziness	2	8
OBJECTIVE EXAMINATION		
Abnormal knee reflexes	65.1	79
Abnormal Achilles	78.1	62
Romberg positive	38	42
Speech defect	15.7	17
Mental symptoms	38.4	38
Paresthesias	55.8	51.3
Ataxia (objective)	36.8	36.3
Bladder (objective)	47.5	20.5

* Reprinted from J. Indust. Hyg. **1**:419, 1920.

is entitled to in making the final decision, and at just what point clinical syphilis may be considered to cross the threshold of identification in an obscure case, presents problems that are unsurpassed in difficulty and in fascination. In time we shall, I hope, by careful statistical evaluation be able to give mathematical expression to some of the elements of the intutitive synthetic instinct and perhaps with a slide rule or formula arrive at some approximation to a diagnosis, much as Dreyer [6] obtains an estimate of the prognosis in tuberculosis by a mathematical computation based on vital capacity.

One of the most interesting impressions one gathers from constant use of multiple diagnostic procedure is that of the extreme rarity of monosymptomatic or truly latent syphilis. In connection with this point we have just completed a survey of an unselected group of Wassermann-fast cases. The polytropism of syphilis, so to speak, stands out strikingly in this group in which all but 10 per cent. of the patients present more than one type of recognizable structural involvement. Such a state of affairs, wholly in keeping with the experience of the postmortem pathologist, holds out much encouragement to the clinical syphilographer, who finds that the efforts of his team are bringing to diagnosis in the living some of the accuracy and comprehensiveness that have so long been monopolized by the prosector for the dead.

IMPORTANCE OF RECORDS IN SYPHILOLOGY

The adequate record is a necessary accompaniment of the newer methods of diagnostic approach. All of us appreciate how much Fournier's encyclopedic knowledge depended on his records. My own enthusiasm on the matter comes, however, from a source nearer home, in the form of H. S. Plummer's mastery of the clinical problems of the thyroid and the conceptions of record which he has incorporated in the "Goiter Sheet" or record form for goiter cases in use in the Mayo Clinic. The record system which Plummer has devised endeavors to set before the examiner in a printed form a pigeon-holed filing case for the disease, into every compartment of which can be dropped either a negative or a positive observation, a measure of time or quantity, or a measure of intensity on a scale of ?, 0, 1, 2, 3, and 4. The examiner begins at the top of the sheet, and, without option or omission, goes through the printed form to the bottom. The data are so indexed by guide letters and numbers that a body of records can be transferred by ordinary clerical help to an abstract sheet which makes the study of clinical relations comparatively simple. Such a system of record, I am convinced, has a permanent investigative value immeasurably greater than the spontaneous or drift record, in which the examiner

6. Dreyer, G.: Investigations on the Normal Vital Capacity in Man and Its Relation to the Size of the Body, Lancet **2**:227, 1919.

follows mental leads and cues to a diagnosis, the written or dictated page setting forth the story of his wanderings. The weaknesses of Plummer's method are largely inherent in the fallibilities, obstinacies, and lazinesses of human examiners, and in the forgetfulness of patients and the inaccuracies of their thoughts and statements. None the less, the advantages greatly outweigh the disadvantages, since the latter affect all forms of medical record alike. A system of record for syphilis will, I believe, be useless for scientific control unless it contains definite information in terms of time and quantity on the following five points:

1. Negative as well as positive findings.

2. The personal resistance of the patient to infection and evidence of individual peculiarities in the course of the disease.

3. Data from which to infer, on definite knowledge in regard to, the strain and peculiarities of the infecting organism.

4. The duration of the disease.

5. The type, duration, and intensity of treatment.

Lacking accurate data on these five points the most complete history of symptoms will be useless for basic investigation, because the fundamental facts regarding seed, soil, and treatment, on which alone a comprehensive study of the crop or outcome can be based, will be lacking. The nature of syphilis itself imposes limitations on such material which will make its accumulation slow. Moreover, such accumulation must await the development of a diagnostic and therapeutic machine which cannot be built up in a year or perhaps even in a decade. In four years of steady effort in this direction with generous facilities I have completed in tentative form only three of four necessary record forms required for this type of work. One of the most potent stimuli that has reached me is the appreciation of Fordyce's remarkable collection of data on the therapy of neurosyphilis. To place the diagnosis and the therapy of syphilis at large on a similar and perhaps even more advanced basis of exactitude appeals to me as a syphilologic ideal of the first magnitude. As one goes over inferior material, the tangible evidence of his own lack of foresight or lack of facilities, he realizes the vital significance of the unmentioned fact in accurate large scale deduction. One understands, too, how the honest substitution of "no data" for the tempting clinical inference or speculation, would leave more than one clinical reputation, his own among the number, puffing for breath. Is it too much to hope that in proportion as we succeed in substituting certainties for probabilities in record we shall build substantial foundations for the clinical syphilology of the future, and introduce into a field of confusion and impression some of the exactitudes and controlled conclusions of actuarial and mathematical science?

I am afraid that I have already exhausted your patience, and for that reason I merely express my willingness to demonstrate to any of you who may be interested the very crude beginnings of a system of record that I am hoping may give me, to some extent at least, the mastery of my own data. The problems that beset one in its development would afford material for another paper and would be much enriched by your suggestions. Before your good will vanishes let me ask you whether it would not be worth while, now or at some future date, provided it has not already been done, for so influential a body as the American Dermatological Association to undertake in behalf of the syphilographer of the future some constructive work on the problems of record in syphilis to which reference has been made? I cannot but believe that in this direction there is need for immediate action to pave the way for many significant future achievements in the revival of clinical syphilology.

SUMMARY

By way of summary, let me say that I have tried to voice my belief that the revival of clinical syphilology calls for a new type of syphilographer, synthetic rather than analytic in temperament, whose qualities as an inspirer of men, a cooperator, interpreter and coordinator, will outrank his merely technical expertness in the minutiae of syphilologic diagnosis. Such a syphilographer will direct in his field the efforts of a highly complex diagnostic organization rather than perform a few special tests. He will become expert in the appraisal of the relative significance of a variety of structural and functional investigations which he does not himself necessarily perform. He will endeavor to give concreteness to the intuitive and he will find in highly developed and systematized records that mastery of data which his synthetic powers require for the attainment of a new type of exactitude and conclusiveness in clinical research.

DISCUSSION

DR. CORLETT was much interested in Dr. Stokes' excellent paper and agreed with what he said. A long time ago he had maintained that dermatology and syphilis go hand in hand, and conceived of the ideal syphilographer as one sufficiently well equipped to handle all these cases, but at the time the ideal seemed impracticable. Many years ago, when the Lakeside Hospital was opened, the trustees decided not to have syphilitic patients in the hospital. Of course, this would have been an ideal situation, but they soon found syphilis among the orderlies and nurses, as well as in general medical and surgical cases in patients who came in for treatment of other ailments.

The board of managers thereupon recognized that syphilis had to be reckoned with, and they organized the Department of Skin Diseases and Syphilis. All cases of syphilis of the eye, nose or throat came through the skin department and were then referred to the different departments for special treatment. Most difficulty was experienced with the Department of Internal Medicine.

the members of which have never worked with that hearty cooperation which the reader of the paper evidently enjoys. Cases of syphilis were then referred back to the Department of Dermatology and Syphilology for systematic treatment, and the patients were discharged by this department. In this way the necessity for these patients to come back in two or three years for further treatment or for treatment of a new outbreak was prevented. The organization was not such as that Dr. Stokes is fortunate to work with, but Dr. Corlett believed that this was the ideal organization, of value alike to the dermatologist and syphilographer.

Dr. Fordyce was much impressed with Dr. Stokes' excellent presentation of this subject. He felt that every one agreed in the proposition that Dr. Stokes had advanced; namely, that more attention should be paid to group medicine. Only in this way could the patient be placed under the best condition to receive the necessary medical attention. The syphilographer should also by such cooperation acquire a more comprehensive grasp of the disease. There are not many trained syphilographers in this country. Many know one phase of this subject but few have a broad knowledge of it in its entire aspect. In institutions organized on the lines of the Mayo Clinic opportunities are afforded the younger men to familiarize themselves with all phases of the disease. Men so trained will eventually exercise a profound impression as a whole. In the institution with which the speaker is connected cooperation is gradually being brought about between the departments of medicine, neurology, ophthalmology, obstetrics, etc. They have, however, not yet reached the stage of the frequent and instructive conferences referred to by Dr. Stokes chiefly because of the time occupied in teaching large classes of students and lack of opportunity for representatives of the various departments to get together.

The only point in Dr. Stokes' remarks that Dr. Fordyce criticized was his reference to the employment of an acute Wassermann system. Why not use an acute Wassermann system? The system employed by the Mayo Clinic might be sufficient but, according to Dr. Stokes, it was rather insensitive. In the early or florid stage of syphilis it is easy to obtain a positive Wassermann reaction with any of the systems used. In treated syphilis great difficulties are found. The cholesterin antigen may give a positive reaction in a certain number of cases while the alcoholic antigen with the ice box fixation may give a certain number of negative results with the same blood. On the other hand, a certain number of negative reactions may be obtained with the cholesterin antigen and with the alcoholic antigen positive reactions. In order, therefore, to detect all cases of syphilis it appeared necessary to the speaker to employ more than one system.

Dr. Schamberg believed that Dr. Stokes had brought a valuable message and that the Association was indebted to him for it. There is perhaps no other disease which is so susceptible to group study and so much benefited by it as syphilis, because, as is well known, there is probably no other disease in which there is such a wide invasion of the whole body as there is in syphilis by the *Spirochaeta pallida*, and such a liability to attack on all of the organs and viscera. He thought the members of the Association would agree with him that special emphasis should be placed on the point that there comes a time in the life of a syphilitic patient when treatment may be lessened in intensiveness or even suspended, even though we know he still suffers from syphilis; attention should be directed to determining the dominant resting place of the spirochetes, the organ or organs particularly attacked by the spirochete at the time—where the spirochete is doing damage. If the patient has a

++++ positive Wassermann reaction, treatment should not ordinarily be suspended. When dealing with a patient of 50, 55 years or older, in whom the roentgenograms indicate that there is no cardiovascular change of any importance and in whom spinal tests indicate that there is no neurosyphilis, he agreed with Dr. Pollitzer and others that it is not desirable to make any intensive effort to reverse the Wassermann reaction, and it might even be wise to suspend treatment. It is a question whether the treatment under such circumstances may not be more of a menace to the patient and the integrity of his organs than is the disease itself.

Dr. Schamberg believed the group study of syphilis to be particularly important when the spirochetes were inducing changes that were interfering with the capacity of certain organs. He thought another phase of the group study was that of congenital syphilis; he felt that the whole chapter of congenital syphilis would have to be rewritten. What has been recognized as congenital syphilis in the past have been the obvious stigmas, such as the Hutchinson teeth, disease of the joints and bones, keratitis, and so on. The profession must realize that children of syphilitic parents may be born in apparent good health and may later manifest abnormalities in the way of persistent anemia, loss of weight, or subtle tissue changes not ordinarily attributed to syphilis. The proof of the nature of these conditions is that only by syphilitic treatment may such patients be restored to health. He believed that tens of thousands of people throughout the country are suffering from anemias, vascular thickenings and other disturbances that are not attributed to the true underlying cause. In his clinic he has a pediatrician who is detailed to examine the children of syphilitic parents especially to determine whether or not they are affected in this manner.

Dr. Pollitzer said that aside from the pleasure he derived from listening to this paper, his principal emotion was one of envy. He could not help envying a man who was in a position to carry out the study of syphilis in the way in which Dr. Stokes had been able to do it. He had been very much interested in the group study of syphilis. It was about ten years since he had attempted to carry out something of this plan of treatment in an institution with which he was at that time connected. Unfortunately, there was not so much altruism, or so much scientific spirit in that institution as there is in the Mayo Clinic. The ophthalmologists, the surgeons, and the genito-urinary men were all afraid they might lose a patient if they sent him to the syphilographer, but he had advocated, in a small crude way, that which is being carried out at the Mayo Clinic. He had had better results in persuading the Department of Health of New York City which had actually made it a part of the sanitary code of the city that in any institution treating venereal diseases, syphilis should be treated in one department. Dr. Pollitzer emphasized the fact that this was a definite achievement and although, like many laws, it is rather inadequately carried out at present, the fact that it is on the statute book makes it a good thing and it is carried out in a good many institutions. Already in several institutions in New York every patient with syphilis is referred to the department of dermatology and syphilis. He believed the importance of this to the patient could not be sufficiently emphasized. The patient who goes to the ophthalmologist or the surgeon may be freed from his eye or bone lesions but his syphilis continues and no one is interested further in the asymptomatic syphilitic. From the standpoint of the patient, Dr. Pollitzer believed the work which is carried out at the Mayo Clinic is of the highest character.

DR. WILE said that everything had been stated by those who had preceded him in appreciation of Dr. Stokes' paper. Dr. Stokes had made order at the Rochester clinic of what Dr. Mayo said was "syphilologic chaos" before he came.

Dr. Wile subscribed to Dr. Fordyce's and Dr. Schamberg's views regarding the Wassermann reaction. He believed that the present test, which was the last word at the moment, would more than likely be supplanted by a more delicate one in the future and that it therefore could not be too heavily leaned on at present. The thing which impressed him most and on which he would like to lay most emphasis was what he deemed the mistake of attempting to connect the Wassermann reaction with treatment. The exact biologic nature of the reaction was as yet unknown to any one. In view of this fact, persistent positives in the presence of intensive treatment were difficult to explain. In still other cases, in which the test was negative, it was still possible that the patient had syphilis. In view, therefore, of the doubtful status of the nature of the reaction, Dr. Wile felt that it could not be with accuracy relied on from the therapeutic standpoint.

DR. IRVINE was very much interested in Dr. Stokes' paper. In his opinion the part that should be particularly emphasized, for the need of the Association, was that the individual members should feel the importance of putting their work on such a basis, particularly those who were in teaching institutions. He doubted whether dermatologists felt the responsibility they should have in teaching syphilis. He was sure there were many schools that did not teach syphilis as it should be taught, and that their students are obtaining a wrong idea both as to the treatment of syphilis and syphilis itself. In trying to establish an organization, such as Dr. Stokes had suggested, they secured the cooperation of the many special departments by making it plain that they could continue to see and demonstrate their patients with syphilis of the eye, ear, etc., and that the department of dermatology and syphilis was interested only in carrying out the routine treatment of such cases and not in teaching syphilis of these various organs. With this understanding, all cases of syphilis are now referred to the department of dermatology and syphilis. Dr. Irvine thought the point Dr. Stokes made of treating group symptoms should be emphasized, as well as the need for the dermatologist to assume the responsibility of the teaching of the proper diagnosis and treatment of syphilis.

DR. PUSEY, while listening to the almost ideal conditions for treating syphilis which Dr. Stokes outlined, found himself paraphrasing an old negro song, "Earth is our abiding place, but Heaven is Stokes' home." When it came to the treatment of syphilis, Dr. Stokes' situation seemed to be one that the rest could only aspire to when they were translated. He thought that Dr. Stokes' outline was interesting and useful in the suggestions which it gave of the value which dermatologists and the profession generally, might obtain from more cooperation in the treatment of syphilis.

DR. STOKES (closing) said one or two points were brought out in the discussion which he wished to take up. First, Dr. Fordyce mentioned using a more acute Wassermann test. He would have explained his sympathy with that idea if he had not felt so hurried. He felt that while the acute Wassermann is best, it is hard for the specialist to realize the crutch which the Wassermann test is to the general man, and that it is really an advantage to be able to say to him as a means of encouraging clinical judgment that only 40 or 50 per cent. of his cases would be positive in the presence of syphilis rather than 100 per cent. Dr. Sanford and Dr. Stokes were considering the introduction of a more sensitive Wassermann test, which they hoped would

identify more latent cases. He had mentioned in his paper on railroad men that a Wassermann test taken between the ages of 17 and 31 would probably get most of the asymptomatic positive Wassermann results that it is possible to obtain.

One of the most interesting studies he had recently undertaken was that of Wassermann positive syphilis which remains persistently positive after long continued treatment. He had found that only 10 per cent. of the cases studied had Wassermann-positiveness as the only evidence of the disease. Involvement of the cardiovascular system was recognized by a sufficiently intensive study as the commonest manifestation of the disease. It was particularly interesting to see how the multiplicity of involvements, the polytropism of the disease emphasized by postmortem findings, could be identified clinically by multiple diagnostic attack.

The matter of record was growing to be one of increased importance in the study and treatment of syphilis. It appeared to him that the Association would be taking a step in the right direction by organizing a committee to consider the subject of record in syphilis and its improvement.

REINFECTION AND CURABILITY IN SYPHILIS

LEO JACOBI, M.D.

NEW YORK

Reports of reinfection in syphilis have been appearing with increasing frequency during the past year or two. The presentation of such a case before a meeting of dermatologists is certain to precipitate a lively and somewhat acrimonious discussion, which, after ranging far afield, usually ends in an impassé. In the confusion of debated issues, however, a sharp cleavage of opinion becomes clearly discernible: one group, which may be called the conservative, holds fast to orthodox views, while the other, less imbued with respect for authority, appears hospitably inclined toward new conceptions. It may be interesting, and perhaps helpful in clarifying our ideas, to analyze in detail the arguments and the method of reasoning employed by the disputants.

As a rule, the validity of reinfection is vigorously contested by skeptics of the old school, strong in the conviction that syphilis, having once invaded the human body, becomes a permanent possession, and can never be shaken off. Their mode of reasoning, reduced to its simplest terms, assumes the form of the following syllogism:

1. Reinfection is impossible in uncured syphilis.
2. Syphilis is an incurable disease.
3. Therefore, reinfection is impossible in syphilis.

Intrenched behind this deduction, they say to their opponents: first prove that syphilis can be cured, and, until you have done so, cease prating about reinfection. To this challenge the progressives reply by a complete reversal of minor premise and conclusion. Granted, they retort, that reinfection can take place only after syphilis has been cured; but reinfection does occur in syphilis, as our cases show: therefore, syphilis is a curable disease.

CURABILITY AND REINFECTION

The antagonism appears to be irreconciliable. Prove that syphilis can be cured and we shall then accept your cases of reinfection, says one side; accept our cases of reinfection and we shall then have proved that syphilis is curable, is the rejoinder of the other.

Yet, in spite of reversed premises and conclusions, both are found tacitly acknowledging the intimate connection between curability and reinfection. Both accept the contingency of the latter on the former as an article of faith.

And it is here, precisely in this reluctance to divorce the two conceptions, that we must look for the real obstacle to a mutual understanding. Strange as it may seem, unanimity on this point is the subtle cause of the entire controversy, and if it could be shown that reinfection is not necessarily contingent on curability, discord would promptly give place to harmony.

It is therefore necessary to submit the proposition: "reinfection cannot take place in uncured syphilis," to a searching analysis, even though it may seem dangerous heresy to doubt a statement so long regarded as almost axiomatic.

Expressed in clear and concrete terms, the proposition in question means that the presence of the *Spirochaeta pallida* (or its transitional forms) in the human body renders the latter unconditionally and absolutely immune against a new invasion by the *Spirochaeta pallida*. Confronted by a thesis so startling and categorical, one naturally expects to find it fortified by every possible proof, and placed beyond the reach of doubt or criticism. As a matter of fact, however, a closer examination of the evidence fails to substantiate such an expectation, and even emboldens one to put the following query: When, where, and by whom has it been indisputably proved that the *Spirochaeta pallida* or its transitional forms must be completely eradicated from the system, before a new invasion by the *Spirochaeta pallida* can occur?

Having squarely faced the issue, we are soon compelled to admit that this "law" derives its alleged validity mainly from assertions made by the great authorities of the past and handed down to us by tradition, assertions which, despite their venerable age, cannot usurp the place of logical argument. In fact, it is difficult to see how adequate proof could have been adduced during the clinical era of syphilology, before the discovery of the *Spirochaeta pallida*, when the only criterion of cure was the absence of clinical manifestations. In our own time, made a little less ignorant by the spirochete and by the Wassermann test, syphilographers nevertheless also have failed to prove that reinfection cannot occur unless syphilis has been cured, or, in other words, that the presence of the parasite renders the host absolutely immune.

The truth or falsity of this allegation could be demonstrated by rigidly conducted experimental inoculations with the *Spirochaeta pallida*, made on persons known to be harboring the parasite.

If long series of such inoculations, carried out under scientific conditions in various stages of the disease, and with various strains of the *Spirochaeta pallida*, were to produce unequivocal results, then, and only then, could we take a definite stand in the controversy. Have such experiments been made on an adequate scale? The answer

can hardly remain in doubt. To be sure, it has been found that auto-inoculation with the virus of the hard chancre is successful during the first week or two, but this knowledge has little value, beyond indicating the approximate time when immunity becomes established. Again, during the the florid period of syphilis, when the system is flooded with parasites, the existence of a strong immunity need scarcely be questioned, though even here inoculations with different strains of *Spirochaeta pallida* might be productive of interesting results.

But it is in the later stages of syphilis, after the conflagration has been reduced to smoldering embers, that we may expect to find a gradual weakening of immunity, and a corresponding susceptibility to a new inoculation. It would be most interesting and instructive, for example, to inoculate cases of general paresis with the specific virus. In this disease, living spirochetes have been found in the brain tissues, but it is quite conceivable that they no longer confer an immunity sufficiently strong to resist a new invasion through the skin or mucous membranes.

Of course, the practical difficulties in the path of such researches on the human subject are well-nigh insurmountable, and we are reduced to the necessity of waiting until the patient takes the matter out of our hands and makes a successful test on his own account. Still, there is an alternative, and that is animal experimentation. Recent studies on animals make the existence of different strains of *Spirochaeta pallida* highly probable, and attempts have been made to classify them, distinguishing a dermotropic variety from a neurotropic, the former showing an affinity for the skin and causing the cutaneous manifestations of syphilis, while the latter, by its selective action on the central nervous system, induces paresis and locomotor ataxia.

Furthermore, it has been found that animals experimentally infected with one variety may be successfully inoculated with the other, developing a new primary chancre. Thus the belief is already beginning to emerge that a new invasion by the *Spirochaeta pallida* is sometimes possible before the old has been completely extirpated. Perhaps the term "superinfection" would be more acceptable to purists when referring to these cases, though reinfection can be defended on etymologic grounds.

Side by side with these results of animal experiments, we encounter in recent literature occasional mention of an attenuated immunity that might make reinoculation successful in the human patient. Thus, while much work remains to be done before the final verdict can be pronounced, it is already becoming more and more evident that the ancient ties that bound together the conceptions of curability and reinfection have at last been effectually loosened, if not entirely severed.

Reinfection is a question of immunity, not of cure. In the future book on immunity, syphilis will be found to occupy a chapter, and reinfection a paragraph. Theoretically, it is quite conceivable that the patient may be cured, that is, completely purged of the *Spirochaeta pallida* or its transitional forms, and yet left in the possession of an absolute and life-long immunity, which would imply the impossibility of reinfection. On the other hand, syphilis might be conceived as an incurable disease, conferring an immunity that gradually declines as the date of the primary infection recedes, until a point is reached at which a fresh inoculation may be successful.

Bearing all this in mind, it will be advantageous henceforth to dissociate the two conceptions of curability and reinfection, and to consider them as separate problems. The answer to the one need not of itself furnish a solution to the other, but each will require its own structure of logical proof.

The first question, that of curability in syphilis, will have to be settled on the strength of clinical, serologic and pathologic evidence. The old syphilographers had to depend almost exclusively on clinical observation. Impressed by the treacherous and protean manifestations of late syphilis, occurring long after infection even in well-treated cases, these authorities show a distinct leaning toward a pessimistic view. Their unfavorable clinical experience hardened into a settled belief that "once a syphilitic, always a syphilitic," and this conception has been transmitted to many of their modern descendants, who consider syphilis an ineradicable disease. In addition to clinical evidence, they can point to such pathologic findings as those of Warthin, who in postmortem examinations demonstrated the presence of living spirochetes in the tissues taken from syphilitic persons who were apparently cured, i. e., gave neither clinical nor serologic evidence of syphilis.

This discovery emphasizes the extraordinary difficulties confronting those who cherish the belief that syphilis is curable and seek for something more tangible in the way of proof than mere conjecture. Indeed, how can one obtain the assurance that a given patient no longer harbors the *Spirochaeta pallida?* Since no reliance can be placed on the absence of clinical phenomena, and since the Wassermann test is not sufficiently delicate and trustworthy, we are left without an absolute criterion of cure and reduced to waiting until future research shall have supplied us with an infallible method of detecting the presence of the *Spirochaeta pallida* in the human body. In the meantime, believers in curability are at the mercy of pessimists, who, refusing to surrender the old dogma of incurability, shift the burden of proof to the side of the optimists.

It is precisely this feeling of helplessness that drives the latter to offer their cases of reinfection as proof of curability—an entirely illogical proceeding, as we have seen. Reinfection does not imply the absence of living spirochetes in the host, but only indicates that the immunity left in the wake of the preceding attack has lost some or all of its original virtue.

Thus the question "Is syphilis curable?" will have to be relegated to the innumerable other problems awaiting future revelations. This is unfortunate, as it deprives the patient of a much-needed solace, and, moreover, leaves the field to the pessimist, who adds to the actual terrors of the disease those of despondency and mental distress.

PRESENT STATUS OF REINFECTION IN SYPHILIS

Let us turn now to the present status of the vexing problem of reinfection in syphilis. Here we find ourselves treading firmer ground. Having emancipated our mind from the old dogma which made reinfection dependent on curability, we are enabled to take an unbiased view of the evidence presented in favor of reinfection. In judging a given case, more weight should be placed on the clinical phenomena than on the intricacies of dialectics and the uncertainties of repeated Wassermann tests. If a patient who had once been infected with syphilis comes to us with a suspicious lesion on the genitals appearing several days or weeks after exposure to infection; if the related inguinal glands become enlarged, hard and painless; if, in due time, secondary manifestations make their appearance, what diagnosis, other than a new syphilitic infection, can be made, even without the finding of the spirochete and a positive Wassermann reaction?

If, in addition, the *Spirochaeta pallida* has been found in the initial lesion, and if, furthermore, the Wassermann reaction, having been negative before the appearance of the new chancre and for some time afterward, now turns to positive, the evidence in favor of reinfection becomes so overwhelming that only one steeped in prejudice and sophistry will remain unconverted.

Caution is necessary in accepting the patient's statement that he has already been the victim of syphilis, and in differentiating the new initial lesion from chancre redux or a gumma; but these and other similar sources of error can usually be eliminated.

It is at this juncture that we again meet the pessimist, who, driven to the wall, takes refuge in the ancient legend, "Once syphilis—always syphilis," and closes his eyes to facts.

It then becomes our duty to inform him that he is laboring under a false conception, or else that he belongs to the category of those perverse persons who have been characterized nineteen centuries ago as having eyes yet seeing not.

The majority of open minded observers have by this time taken their stand in the controversy, and I am on the side of those who regard reinfection as definitely proved.

SUMMARY

In conclusion, our analysis may be summarized as follows:

1. The question, "Is syphilis curable?" cannot be answered definitely in the light of our present knowledge.

2. The occurrence of reinfection in syphilis may be accepted as an established fact.

3. Reinfection, however, is by no means evidence of curability.

These two conceptions do not stand and fall together, as many believe; they are not contingent on each other, and should be dissociated in the interest of clear thinking and unbiased judgment.

EXPERIENCE WITH SODIUM DIARSENOL

PRELIMINARY NOTE

FRANKLIN R. WRIGHT, M.D., AND HENRY E. MICHELSON, M.D.
MINNEAPOLIS

We have used ten tubes of sodium diarsenol furnished by the Diarsenol Company of Buffalo and thought that this preliminary note might be of service to others who wish to use this product. The drug was used in four cases.

REPORT OF CASES

CASE 1 (No. 261).—A man, aged 36, single, presented himself on June 8, 1920, with four small indurated papules on the corona and an ulceration at the frenulum. *Spirochetae pallidae* were easily demonstrated. The Wassermann reaction was negative. On June 8 he was given 0.45 gm. of sodium diarsenol; on the 9th he received 0.6 gm. and on the 10th he again received 0.6 gm., that is, he received three doses on each of three successive days. He had no reaction and the therapeutic effect was equal to that of any preparation we have used. On June 14 he reported for mercury treatments and the papules were entirely healed.

CASE 2.—A man, aged 30, presented himself on June 8, 1920, with an ulcer the size of a nickle on the mucous membrane surface of the prepuce. The inguinal lymph nodes were enlarged, *Spirochetae pallidae* were easily demonstrated and the Wassermann reaction was negative. On June 8 he received 0.45 gm. of sodium diarsenol and on the 9th he received 0.6 gm. In the evening he suffered with severe nausea and vomiting. This may have been due to the fact that he disobeyed orders and ate a rather heavy meal. The dose was not repeated until June 11 when he again received 0.6 gm.; this time there was no reaction. He reported again on June 15. The ulcer was diminished to one third its original size. Again the therapeutic effect was all that could be expected.

CASE 3.—A man, aged 23, presented himself on June 15, 1920, with two indurated ulcers, one on the glans and the other on the opposing mucous membrane surface of the prepuce. *Spirochetae pallidae* were easily demonstrated. The Wassermann reaction was positive. Pallor and general malaise were marked and the inguinal lymph nodes were much enlarged. On June 15 he was given 0.45 gm. of sodium diarsenol. He complained that after four hours he was seized with a severe chill and severe depression. He felt somewhat dizzy but had completely recovered on the following afternoon. On the next day the lesions were distinctly flattened. On June 17 he received 0.6 gm. without any particular reaction.

CASE 4.—A young man, aged 19, presented himself on June 8, 1920, with a small eroded papule on the glans. *Spirochetae pallidae* were present. He received that evening 0.6 gm. of neosalvarsan (Metz). He did not report again until June 11, when the lesion was one-half its presenting size. He then received 0.6 gm. of sodium diarsenol and was not seen again until June 15. The lesion was then completely healed and he had not had any particular reaction with the last injection. All of the injections were in 20 c.c. of sterile distilled water.

We contemplate using 500 tubes in the university clinic and hope to publish detailed reports later.

THE ACTION OF RADIUM ON A VARIETY OF CUTANEOUS CONDITIONS

DOUGLASS W. MONTGOMERY, M.D.
AND
GEORGE D. CULVER, M.D.
SAN FRANCISCO

The use of radium in cancer, whether for amelioration of the symptoms or cure of the disease, is so beneficent that it has overshadowed its use in a great number of other affections. In the conditions discussed it has afforded us valuable service.

PERSISTENT FISSURES OF THE NARES AND LIPS

As the result of catarrh, cracks may form in the nares, especially frequently in the anterior angle. These are often associated with folliculitis of the vibrissae. The usual infective agent is a streptococcus, and it often gives rise to localized attacks of erysipelas, and after a time, to permanent redness of the nose. In fact, it is one of the principal causes of red nose. The best routine treatment is the use of boric acid fomentations, and the employment of a 12 per cent. calomel ointment, under which almost all cases will clear up. Some cases, however, are refractory.

A man, 37 years of age, had been under the care of a competent physician for this condition in the left nostril for one year before coming to us. The refractoriness in this case may have been due to inflammatory induration and to streptococci lying latent deep in this induration, as they are now known to do. We were confronted by an unusually stubborn case, and in addition to the boric acid fomentations and the calomel ointment, we employed radium.

On July 21, two 25 mg. tubes, screened with a silver tube of 0.35 mm. wall thickness and a rubber cot, were placed in the left nostril for fifteen minutes. By August 22 the condition was much improved, but there was still a little sensitiveness at the tip of the anterior angle. An 11 mg. radium plaque, shielded with a rubber cot, was placed over this region for five minutes. By September 15, the man had completely recovered, and we have heard of no relapse.

In this case it might be objected that radium with 0.35 mm. silver screening for fifteen minutes would have no effect—that the screening was too heavy and the time too short. This tube, however, was itself highly radioactive as the radium was constantly kept in it.

Another instance of fissuring occurred in a soft, pulpy man of 49, weighing 205 pounds, who had been troubled with the nasal condition for the previous three months. He was also afflicted with cracking and irritation of the

perineum and anus. After a preliminary treatment which proved ineffectual, radium was used in both situations. The relief was prompt; the anal discomfort disappeared within twenty-four hours.

LUPUS ERYTHEMATOSUS

To us one of the chief inducements for using radium was its favorable effect on that stubborn affection, lupus erythematosus. Its effect is greater than could be expected, for the eruption of lupus erythematosus is only a symptom and the real origin of this symptom lies in some hitherto not demonstrated internal affection.

We have found that the best results are obtained with very slight screening, and after an application of long duration. We employ a standard sized plaque which contains 11 mg. instead of 10 mg. of radium element, with a screen of two thicknesses of writing paper, for thirty minutes. Distance must always be considered an especially excellent screen, and distance is often secured by interposing cellulose, such as paper or felt. In lupus erythematosis, however, too great a distance is not desirable. A patient, an intelligent young man, deeply interested in his trouble and in the effect of radium on it, noted that the areas treated with the plaque in quite close contact with the affected surface, only screened with two thicknesses of writing paper, produced better results than when a thicker screen was interposed. A lead shield placed about the patch also interfered with obtaining the best results. Apparently close contact and wide inclusion of the margins, so as to radiate well beyond the visible border, is desirable.

DYSTROPHY OF THE NAILS IN SEBORRHEIC ECZEMA AND PSORIASIS

Sometimes in the disease above mentioned, the deformities of the nails are the most distressing lesions, as in the case of a dentist who thought he would have to change his occupation because his nails were so ugly and so difficult to clean.

On Sept. 27, 1919, a woman consulted us concerning dystrophy of the nails. The trouble had begun one year before as a redness and crusting in the nail fold. The fourth and fifth fingernails of the right hand and the fourth finger of the left hand were affected. Besides this, she had seborrheic eczema of the nasolabial folds, patches of psoriasis on the right elbow tip and on the right leg just above the external maleolus.

Any one acquainted with the obduracy of these cases of seborrheic paronychia before the introduction of the roentgen-ray or radium will appreciate the results we have obtained through these mediums. In addition to general treatment, we employed lightly screened radium plaques over the nails for short periods of time. After a fairly strong reaction, the nails grew out normally.

LICHEN HYPERTROPHICUS

The eruption of lichen planus is usually so widespread that roentgen-rays are much more easily utilized than radium, but recently we had a case of "white spot" disease with two hypertrophic lichen papules on the back of the neck. These papules were each 11 mm. long and 6 mm. broad. They were raised, oval, with a pale, rather milky colored border, and a rough center studded with follicular openings filled with small, horny comedos. There were pale, milky bands running across the top of the papules between the follicular openings. Radium, lightly screened, acted well on these papules, and caused their disappearance. We doubt whether roentgen rays would have acted as well.

VENEREAL WARTS

A man, 21 years of age, while under treatment for syphilis, developed papillomas in the anterior part of the urethra. A 25 mg. tube of radium, enclosed in its silver capsule, 0.35 mm. wall thickness, and covered with one thickness of writing paper and one thickness of zinc oxid adhesive plaster, was inserted and kept in place for forty-five minutes. This was done April 8, 1919, and by April 24 the papillomas were disappearing rapidly. In a short time they cleared up entirely, leaving no trace.

PATCHES OF INDURATED ECZEMA

There are patches of indurated eczema in which the induration and the pruritus are the main clinical features. These may be limited in extent, and as refractory to treatment as they are limited. The following case is a good example of this annoying affection.

A woman, 64 years of age, suffering from aortic regurgitation with marked pulsation in the neck, an enlarged liver, and sluggishness of the bowels, consulted us on account of a lump on the inner surface of the right natis. It was red, raised, rounded, sharply bounded, but was evidently eczematous and not neoplastic in its nature. It was not a keloid. We were able to reassure the patient in regard to tumor formation, but the prognosis as regards the cure of these cases is anything but good. As these patches are very itchy, the outlook is not cheerful. We were, however, able to control entirely the pruritus with salicylic acid plaster mull (5 per cent. strength). The thickening remained, however, and two or three days after discontinuing the use of plaster the pruritus would return. By April 27, 1917, the affection had improved, but there was still a small edematous, red patch left, which we knew would rapidly assume its original dimensions and irritability on removal of the salicylic acid plaster. We were frankly discouraged as far as the hope of achieving a permanent cure was concerned.

We were preparing the patient for a life-long use of this remedy when we fortunately employed radium. On April 27, 1917, after eighteen months of other treatment, a radium plaque containing 11 mg. of radium element was placed on the patch, shielded with one thickness of writing paper and one of rubber tissue, and retained ten minutes. This completely relieved the itch-

ing, and there was no trace of the induration on June 12, 1917. To make sure, however, we again used this same plaque for ten minutes, screened with 0.50 mg. of aluminum. There has been no return of the condition since that time.

COMMENT

These few cases give some idea of the wide application of this remedial agent in diseases of the cutaneous envelope. The ease of its application, its painlessness and its excellent results make it one of the most valuable additions to the dermatologist's list of effective remedies.

Correspondence

"THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION"

To the Editor:—I have read with much interest Dr. Herman Goodman's article on "The Effect of Mercury Salicylate on the Wassermann Reaction," in the August number of the *Archives of Dermatology and Syphilology*. I thought all syphilologists were past that milepost of knowledge which marks the use of liquid petrolatum as a vehicle for intramuscular injections. It has repeatedly been shown that the material is not absorbed, and that about all the physician gets is a paraffinoma for his pains.

I think Dr. Goodman also erred in the matter of dosage. Few of us would expect to secure permanently beneficial results following one grain doses of mercury salicylate, injected at intervals of one week, even if an absorbable medium were used.

I have been employing mercury salicylate, in an olive oil and lanolin emulsion, for more than twelve years, and while I occasionally branch off and try some other highly recommended preparation, I have invariably returned to the old standby, for I am convinced that when properly employed it is one of our most potent and reliable remedies in combating syphilis.

RICHARD L. SUTTON, M.D., Kansas City, Mo.

"THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION"

To the Editor:—Although Dr. Sutton may very properly criticize the method of using mercury salicylate described in my article, "The Effect of Mercury Salicylate on the Wassermann Reaction," on the ground that, in his opinion, the dosage and vehicle are objectional, it is hardly accurate to suggest that the method is antiquated and not in use by modern syphilographers.

As to the vehicle: Liquid petrolatum is a menstruum which has been and is being largely used. Stellwagon, Hazen, Ormsby—to take the first illustrations that come to hand—all give liquid petrolatum or its equivalents as a vehicle for mercury salicylate. The "Army Manual of Treatment of Venereal Diseases" gives the same menstruum, as does the Public Health Service edition of that manual.

As to dosage: Perhaps no one in this country or elsewhere has given so much attention to the safe dosage of mercury as have Schamberg and his coexperimenters of the staff of the Dermatological Research Laboratories. In a pamphlet on the treatment of syphilis just issued from these laboratories the following statement on this subject appears: " . . . the insoluble compounds, if used at all, should be limited to one grain doses . . ." Elsewhere the same authors say: ". . . A word of caution must be sounded for the insoluble mercurials; administered as they usually are, once a week, they are sure to accumulate in the body . . ."

HERMAN GOODMAN, M.D., New York.

Abstracts from Current Literature

THE STRUCTURE OF NORMAL FIBERS OF PURKINJE IN THE ADULT HUMAN HEART AND THEIR PATHOLOGICAL ALTERATION IN SYPHILITIC MYOCARDITIS. O. Van Der Stricht and T. Wingate Todd, Johns Hopkins Hosp. Rep. **19**:1, 1920.

This monograph, of considerable interest to the worker in the pathologic anatomy of syphilis, presents the following points which relate to the changes in the structure of the fibers of Purkinje produced by syphilis. Longitudinal cleavage of Purkinje cells is manifested in the normal heart, but in the syphilitic organ this condition is so marked that it must be considered pathologic. Because of the hypertrophy of the interstitial connective tissue the cleavage affects a much greater number of Purkinje cells and constitutes the most important factor in the atrophy and disappearance of many of these elements. In the pathologic heart the connective tissue septum (endomysium) of cleavage can undergo a considerable thickening and invade the neighboring daughter cells in its turn, subdividing them into smaller symmetric or asymmetric elements, the diameter of which hardly surpasses that of a smooth muscle cell. These markedly atrophied cells still possess, when they have retained the features of Purkinje type, a myofibrillar cortical layer and an axial sarcoplasmic zone between which there often appears an internal cytoplasmic membrane.

The atrophied elements in their turn may undergo cleavage into smaller fragments which may be nucleated or devoid of nuclei. The latter type represents the last vestiges of the Purkinje cell before its disappearance or complete sclerosis. The pathologic cleavage of the Purkinje cell may be accompanied by amitotic division of the nucleus induced by the extension of the endomysial septum. In certain cases blood capillaries seem to play a predominant rôle in the invasion by the endomysium. Purkinje cells present a special morphology in accordance with the special functions which they fulfill. They possess the power of evolving and of transforming themselves into cardiac elements even in the normal state, but in the pathologic condition this process of transformation may become so accentuated that it appears as possibly constituting an important factor in the production of derangements of cardiac rhythm. Surrounding the Purkinje cells laterally there is a very thin endomysial membrane continuous with the cleavage partitions appearing in the division of a mother cell. It should be considered as a production not of the peripheral cytoplasm of the muscular cell but of the neighboring endomysium. It corresponds then to a kind of false sarcolemma. In the pathologic condition this sarcolemma may undergo considerable hypertrophy and with the sclerosed interstitial connective-tissue it forms a second very important factor which in the process of cleavage may exercise a marked influence toward the atrophy of the Purkinje elements.

The endocardium which covers the different segments of the atrioventricular bundle is of variable thickness. In the normal heart it is notably thicker in the right atrium than in the ventricles and it is thicker in the left ventricle than in the right. In the syphilitic heart it undergoes considerable hypertrophy in the ventricular areas especially in the left ventricle. It therefore participates in the sclerotic process which affects the atrioventricular

bundle. Elastic fibers are very abundant in this endocardium and in certain locations they produce three successive networks which tend to become transformed into fenestrated elastic membranes. The increase in diameter of the pathologic endocardium is due not only to the formation of new collagenous bundles, but also to the production of numerous elastic elements. The endocardium related to the different segments of the atrioventricular bundle may include isolated scattered smooth muscular fibers, isolated bundles or sometimes more or less continuous layers of smooth muscle fibers. In the normal heart these are much more numerous in the atrium than in the two ventricles and a little more numerous in the left ventricle than in the right. In the syphilitic heart they are markedly diminished in number in the two ventricles and even in the atrium. There seems no doubt that the sclerotic process has exercised a considerable influence toward their reduction in number.

In the pathologic heart there exist traces of a slight diffuse inflammation along the majority of the segments of the atrioventricular bundle and its superficial endocardium. At certain levels in the left ventricle are to be observed centers of much more marked infiltration.

Sclerotic lesions of the interstitial connective tissue and of the small arterial branches, atrophy of the Purkinje fibers and diffuse inflammation are much more accentuated in the ventricles than in the atrium and particularly in the left ventricle.

SENEAR, Chicago.

SPECIFIC AORTITIS. W. D. REID, Boston M. & S. J. **183**:67 (July 15) 1920; **183**:105 (July 22) 1920.

The author makes an exhaustive study of the subject and appends an excellent bibliography. He devotes considerable space to the pathology of the condition, both from a study of fifty-four necropsies at the Massachusetts General Hospital since the spirochetes in aortic tissue were demonstrated there for the first time in this country in 1909, and from a study of the literature.

This disease was present in 3.5 per cent. of the total number of necropsies at this hospital. The author's clinical material is derived from a study of the records of 105 patients treated for the disease at the same hospital. His conclusions are somewhat as follows: Syphilitic disease of the aorta is one of the most common and most serious findings in all cases of acquired syphilis. The lesion is essentially a mesortitis beginning first about the vasa vasorum and is a manifestation of active syphilitic disease, the spirochetes having been demonstrated in the lesion in eleven of his cases. The aortic process frequently extends to the aortic cusps and it has been shown that relatively often there is accompanying myocarditis of spirochetal origin. Aortic roughening and regurgitation, dilatation or aneurysm of the aortic arch and angina pectoris are common in syphilitic aortitis. Nonsyphilitic forms of aortitis are rare.

He discusses the subjective symptoms, shortness of breath, substernal pain, cough, and palpitation and takes up the physical signs under the subdivisions of inspection, palpation, auscultation, Wassermann reaction and roentgen-ray examination. Many cases may be called latent because symptoms are absent. Such cases are commonly undiagnosed until disclosed perhaps in a routine roentgen-ray examination. There is no one point on which diagnosis should be based, but only after a study of all the facts in a given case should a decision be rendered. Every case of cardiac disturbance of obscure origin, especially if the patient is a young adult and if there are signs of involvement of the aortic valve, should immediately suggest the possibility of syphilitic causation. A

positive Wassermann reaction is of confirmatory value but is frequently absent. Roentgen examination, though unreliable in early cases, gives perhaps the most reliable findings. Syphilitic aortitis evidences a tendency to progressive impairment of the heart and aorta and is therefore of serious import. Treatment should be directed primarily toward killing the spirochetes in the aortic lesions. The use of both mercury and arsphenamin is advocated. Decompensation of the heart is to be treated as in that of nonsyphilitic origin.

The need for early diagnosis is emphasized, as well as the fact that there should be a greater willingness on the part of clinicians to make a tentative diagnosis and resort to a therapeutic test. Along such lines lies the greatest hope for improvement in the mortality rate of this disease.

LANE, Boston.

UEBER DIE SACHS-GEORGISCHE AUSFLOCKUNGSREAKTION (THE SACHS-GEORGI PRECIPITATION REACTION). LEO KUMER, Wien. klin. Wchnschr. **33**:562, 1920.

Although the technic of the Sachs-Georgi precipitation test for syphilis is apparently simple enough, it requires some skill and practice. In addition, not every antigen prepared serves the purpose; in one series only one of three extracts prepared similarly gave the reaction. The method of diluting the antigen is still under study, and one cannot say at this time whether rapid or slow dilution will give the proper test.

Clinically, the reaction has been reported for over 30,000 trials. In few cases of florid secondary syphilis has the reaction failed to be positive. Several nonspecific cases have, on the other hand, been reported as giving positive results. A modification in the hours of incubation is claimed to nullify this objection. Kumer has performed over 2,200 Sachs-Georgi tests, paralleling them with the Wassermann reaction. Eighty-one per cent. gave identical results, and if those with minor differences were included, the percentage of equivalent results reached ninety-one. In his first series of 1,245 cases, there were fifty-five spinal fluids: forty-eight gave negative Wassermann and Sachs-Georgi reactions; two gave positive Wassermann reactions and negative Sachs-Georgi reactions, and five gave negative Sachs-Georgi reactions and weakly positive Wassermann reactions. Study of the history and clinical examination showed that the Wassermann reaction persisted longer than the Sachs-Georgi. The assertion has been made that the Sachs-Georgi reaction precedes the Wassermann in primary syphilis. The authors had forty-four initial lesions; in five there was an agreement as to strongly positive, in six an agreement as to weakly positive, in twenty-one an agreement as to negative. In one case a positive Sachs-Georgi reaction paralleled a negative Wassermann reaction; seven patients with negative Sachs-Georgi reactions gave positive Wassermann reactions; and in three cases the differences were not marked.

The Sachs-Georgi is a valuable reaction; it cannot as yet be substituted for the Wassermann reaction, but is the most desirable test to parallel the Wassermann.

GOODMAN, New York.

A COMPARATIVE STUDY OF THE TRYPANOCIDAL ACTIVITY OF ARSPHENAMIN AND NEOARSPHENAMIN. J. F. SCHAMBERG, J. A. KOLMER and G. W. RAIZISS, Am. J. Med. Sc. **160**:25 (July) 1920.

The authors utilized rats infected with a virulent strain of *T. equiperdum* to determine the smallest amount of the drugs in question necessary to sterilize

the animals inoculated with an approximately known number of organisms. The rats were inoculated twenty-four hours before medication was commenced, using doses of arsphenamin varying from 0.005 to 0.02 gm. per kilogram of rat and neoarsphenamin in doses of 0.008 to 0.04 gm.

The average minimal sterilizing dose of twenty-one compounds of arsphenamin from six different laboratories was found to be 0.023 gm. per kilo of rat while the average for neo-arsphenamin under the same conditions was 0.04 gm. per kilo of rat. The trypanocidal activity of the various compounds was found to vary in the same manner as the toxicity.

According to the results of these experiments, 0.6 gm. of arsphenamin equals 1.05 gm. of neo-arsphenamin in therapeutic activity, and the authors consider 1 gm. of neo-arsphenamin to have a greater margin of safety than 0.6 gm. of arsphenamin although arsphenamin has a trypanocidal activity which is 1.74 times greater than neo-arsphenamin.

JAMIESON, Detroit.

COMPARATIVE STUDIES OF THE TOXICITY OF ARSPHENAMIN AND NEO-ARSPHENAMIN. J. F. SCHAMBERG, J. A. KOLMER and G. W. RAIZISS, Am. J. M. Sc. **160**:188 (Aug.) 1920.

Although the "lethal toxicity" of the drugs in question can be determined by experiments with rats and mice, these animals do not show any of the effects of the so-called "nitritoid crises" in man, the latter being due to some factor either in preparation or to the unidentified toxic substance "X."

These experiments show that arsphenamin injected intravenously by the method described can be tolerated by rats in amounts of 0.105 gm. per kilo of body weight which is equivalent in man to twelve times the usual maximum dose of 0.6 gm. By similar comparison with neoarsphenamin the rat toleration is 0.18 to 0.3 gm. or the equivalent of nineteen times the maximum (0.9 gm.) usually employed.

Subcutaneously arsphenamin is tolerated in rats in larger doses than neoarsphenamin, in the proportion of 0.342 gm. to 0.177 gm. of the latter. This proportion is reversed when mice are used.

The authors conclude that the margin of safety is considerably in favor of neo-arsphenamin in the treatment of syphilis.

JAMIESON, Detroit.

THE SIGNIFICANCE OF SYPHILIS IN PRENATAL CARE AND IN THE CAUSATION OF FETAL DEATH. J. WHITRIDGE WILLIAMS, Bull. Johns Hopkins Hosp. **31**:141 (May) 1920.

A study of 302 fetal deaths occurring in 4,000 consecutive deliveries in the Johns Hopkins Hospital, including deaths during the last ten or twelve weeks of pregnancy and the two weeks immediately following delivery, revealed that syphilis was responsible for 34.44 per cent. of the entire number and that it caused more deaths than any other single factor. Of the 302 deaths, ninety-nine occurred in white and 203 in black infants, an incidence of 5.4 and 9.4 per cent., respectively. Syphilis was noted in 104 cases, in eighty-nine the diagnosis was confirmed by necropsy with the demonstration of spirochetes in the fetal tissues, while in the remaining fifteen it was based on clinical findings in the child, or on the presence of syphilitic lesions in the placenta associated with a positive maternal Wassermann reaction. Syphilis was the cause of 12.12 per cent. of fetal deaths of white persons and of 45.23 per cent. of black.

Of the 4,000 women under consideration, there were 1,839 white and 2,161 black women in whom a positive Wassermann reaction was present in 2.48 and 16.29 per cent., respectively. There were 105 additional women in whom the Wassermann reaction was negative, but in whose histories syphilis was mentioned. These women were divided into three groups according to amount of treatment before delivery: (1) no treatment; (2) inefficient treatment, and (3) four to six injections of arsphenamin and mercurial treatment with the result that the Wassermann reaction became negative and remained so. In these three categories there were 157, 103 and 163 patients, respectively, and the results of the treatment are shown by the fact that in the first group 52 per cent. of the children were born dead or presented some evidence of syphilis, as compared with 37 per cent. in the second group and 7.4 in the third.

All obstetric patients should be encouraged to register not later than the third or fourth month of pregnancy, a routine Wassermann test should be made at the first visit and in case the result is positive, intensive treatment should be started immediately. In this way syphilis will be reduced from the most important cause of fetal death to one of the least frequent.

ZIMMERMAN, Baltimore.

DAS BEHANDLUNGMASS DER REZENTEN LUES (MEASURED TREATMENT OF RECENT SYPHILIS). ALFRED BRANDWEINER, Wien. klin. Wchnschr. **33**:558, 1920; continued **33**:583, 1920; concluded **33**:608, 1920.

A routine treatment for all cases of syphilis cannot be practical. One must consider the individuality of the patient and his infection. Recent syphilis should be divided into two classes: a period prior to the stage of positive serology and a stage after the Wassermann reaction has become positive. Patients of the second class should be regarded as secondary syphilitic patients. The Wassermann test should be made at each vein puncture, and if positive at any time during treatment, the patient belongs to the second class even if the Wassermann reaction before treatment was begun had been negative.

Ideals in treatment have changed with the advent of arsphenamin and the Wassermann reaction. Freedom from clinical symptoms is not enough to judge the efficacy of the therapy, and abortion of infection is possible in the early cases.

Brandweiner used the neosalvarsan brand of arsphenamin in this study, using mercury in conjunction either intramuscularly or by rubbings. In cases in which the diagnosis was made by the demonstration of the *Spirochaete pallida,* treatment was begun with 0.3 or 0.45 gm. The second injection was given after an interval of from five to seven days, and if no untoward results had followed the first, the dose may be 0.6 gm. The mercury treatment is begun after the second neo-arsphenamin injection. The neo injections are contained at weekly intervals, using 0.6 gm. until 26 decigrams have been administered. After an interval of two months the treatment is repeated in all cases to be certain that there be no recurrence either clinically or serologically. In the Wassermann positive cases, a third course is recommended.

Brandweiner studied his cases with the view of determining the relation between the quantity of treatment and recurrences. On an average, the difference of 0.5 gm. of neo-arsphenamin was all that lay between success and failure. For example, thirty-two patients received an average of 2.85 gm. of neo-arsphenamin and remained asymptomatic, while twelve other patients who

received an average of 0.325 gm. of the same drug showed secondary manifestations. The mercurial treatment was fourteen rubs and five injections in the first group, and fifteen rubs and five injections in the second.

Neurorecidive lesions may be prevented by local treatment of the chancre. Excision of the lesion and mercurial applications to the site appears to be a procedure to be recommended. If the localization prevents excision, mercury should be applied and kept up even after the sore has disappeared and until all evidence of infiltration has disappeared.

GOODMAN, New York.

PELLAGRA. FRANCIS D. BOYD, Edinburgh M. J. **24**:6 (June) 1920.

Pellagra is a disease which is of enormous importance from an economic standpoint in Italy, Spain, the Middle East, Lower Egypt, Northern China and other parts of the world. It is estimated that in Roumania alone as many as 100,000 cases of pellagra have occurred in one year. There are far more cases in Great Britain than is generally recognized.

In an inquiry into the health of the Turkish prisoners of war, Boyd and his collaborators found that pellagra was prevalent in November, 1918, over 1,500 patients with this disease being admitted to the hospital.

The characteristic early features of the disease are pigmentation and dryness of the skin. The pigmentation and dryness were first noticeable on the backs of the hands and on the face. On the face, commencing on the nose, it spread out over the cheek in a bat-wing outline. There was a band of pigmentation around the neck and extending down the sternum like a cravat. The dorsa of the feet showed dryness and pigmentation. Points of pressure showed pigmentation and scars were deeply pigmented. In acute cases the pigmentation developed into erythema, and even into ulceration. The backs of the hands appeared raw and deep cracks developed. The appearance of the tongue was characteristic. At first somewhat furred, it rapidly lost the epithelium and had the appearance of moist raw meat.

Early in the disease the hydrochloric acid of the stomach was diminished, to become completely lost in the fully developed clinical picture. The systolic blood pressure was found to fall as low as 78 in acute cases.

As a result of the clinical and laboratory studies, Boyd concludes: (1) that the clinical features of the disease are those of profound suprarenal inadequacy; (2) that there is no evidence of any specific protozoan or bacterial infection; (3) that digestive disturbance accompanied by defective secretion of hydrochloric acid leads to disturbance of pancreatic functions, defective digestion, and malassimilation of protein and fat; (4) that there appears to be an intimate connection between biologic protein in the diet and pellagra; (5) that the disease produces a loss of resistance to the invasion of bacterial and protozoan disease, and is therefore a contributory factor to a high rate of mortality.

LEVIN, New York.

CHRONIC FIBROID SUBCUTANEOUS SYPHILOMATA OF THE LEGS, ASSOCIATED WITH CHRONIC PERI-URETHRAL INDURATION IN THE PENIS (SO-CALLED "INDURATIO PENIS PLASTICA"). F. PARKES WEBER, Brit. J. Dermat. & Syph. **32**:173 (June) 1920.

Weber describes the case of a man, aged 60 years, who had had gonorrhea at the age of 20, and who had a positive Wassermann reaction, although there was no history of syphilis. There was a peri-urethral nodular infiltration in the distal half of the penis, apparently situated in the fibrous tissue of the

septum between the corpora cavernosa. The patient likewise presented multiple subcutaneous, rather hard nodules on his lower extremities. The nodules were painless and hardly tender to pressure, varying in size from a hazelnut to a chestnut. These had been present for seven or eight years, one of the nodules, lying deep in the subcutaneous fat and close to, though not actually adherent to the capsule of the knee-joint. Macroscopically it seemed to consist of hard, white fibrous tissue, irregular in outline, and not encapsulated. Microscopically there was seen a dense mass of fibrous tissue, surrounded by and including numerous foci of chronic inflammatory small cell infiltrations.

Weber thinks that this proves that the growths are not true fibromas, and that they are due to some kind of chronic inflammation, probably syphilitic, and he interprets them as probably tertiary syphilitic gummas which have become fibrous without undergoing a true gummatous or necrotic change. For the author the chief interest in this case lies in the association of the subcutaneous chronic fibroid syphilomas of the legs with the chronic peri-urethral induration in the penis, for he considers that the latter condition may also be in some cases a fibrous change of syphilitic origin. He discusses this chronic peri-urethral induration in detail.

SENEAR, Chicago.

DIE PATHOLOGIE UND THERAPIE DER SYPHILIS IM LICHTE DER MODERNEN FORSCHUNGSERGEBNISSE (THE PATHOLOGY AND TREATMENT OF SYPHILIS IN THE LIGHT OF MODERN INVESTIGATIONS). E. FINGER, Wien. klin. Wchnschr. **33**:373, 1920.

A presentation of the advances in the knowledge of the bacteriology, serology and specific medication of syphilis. The value of clinical knowledge of early syphilis is emphasized, and the correlation of laboratory and physical examination is insisted on. In primary syphilis prior to the Wassermann positive period, treatment consists of thirty mercury rubs, or ten injections of mercury salicylate or calomel, and five or six moderate doses of arsphenamin or neo-arsphenamin. Ordinarily this suffices, although it is a good measure to examine the blood by the Wassermann test. Once the Wassermann reaction is positive, even if no secondary symptoms are apparent, the case is to be considered one of secondary syphilis. The treatment in this stage consists in repeated courses of arsphenamin and mercury at intervals of three or at most four months. In some cases of failure to reduce the Wassermann reaction by arsphenamin and mercury, success may follow the injection of milk and other substances which induce a temporary rise in temperature. If the spinal fluid reaction is positive, efforts should be made by intensive treatment to negative the abnormal findings. Intraspinous treatment is still questionable. The new advances in the pathology of syphilis are bringing up problems in treatment that are still beyond our knowledge.

GOODMAN, New York.

MALADIE CUTANEE PROVOQUEE PAR UN PEDICULOIDES TROUVE DANS UN CHARGEMENT D'ORGE ARRIVANT AU HAVRE (CUTANEOUS DISORDER PRODUCED BY A PEDICULOIDES FOUND IN A CARGO OF BARLEY RECEIVED AT HAVRE). LOIR and LEGANGNEUX, Paris méd. **10**:140 (March) 1920.

Loir and Legangneux describe an outbreak of an eruption among men engaged in unloading barley from a Japanese vessel. Sixty-three men devel-

oped the eruption which affected the covered parts, and it was found that in those wearing a belt the thighs were not affected, while the opposite was true among those wearing suspenders. Sacks of wheat had first been unloaded from the vessel without incident, and it was only after they had unloaded barley that the men began to complain of intense itching. Examination of the barley and the dust from the sacks disclosed a parasite belonging to the family of Tarsonemidae and to the group of Pediculöides. Under antiscabetic treatment improvement was rapid and sulphur fumigation of the cargo prevented further outbreaks of the eruption at Havre. The authors review the record of outbreaks of like nature at Havre, and in conclusion give directions for preventing future attacks.

SENEAR, Chicago.

THE RELATIONSHIP BETWEEN ARSENICAL POISONING AND YPERITIS. J. E. R. McDONAGH, Brit. J. Dermat. & Syph. **32**:188 (June) 1920.

McDonagh notes that in cases of arsenical and mustard-gas poisoning three points common to both stand out: 1. The delayed onset of symptoms of intoxication. 2. The fact that such symptoms may vanish and then reappear. 3. The frequency with which a bacterial infection complicates the worst cases.

After a detailed and highly technical comparison of these two conditions he concludes that:

1. Arsenic is the cause of arseno-benzene poisoning, and sulphur of mustard-gas poisoning.

2. Arsenic and sulphur act as catalysts, which fact prevents their ready excretion and induces the recurrence of the symptoms of intoxication.

3. Metals and non-metals are antidotes for each other.

4. Metals and non-metals act therapeutically through the host's resisting substance, which latter they destroy if prescribed in overdose, thereby enabling other organisms which are normally kept in check to multiply until they kill the patient.

SENEAR, Chicago.

ECZEMA OF THE VERMILION BORDER OF THE LIPS. DOUGLASS W. MONTGOMERY and GEORGE D. CULVER, Med. Rec. **98**:141 (July) 1920.

The authors are not sure that any of the cases were of a true eczema type. They divided the various types into:

1. Catarrhal inflammation of the red of the upper lip. This condition often leads to swelling and deformity as a result of pyogenic infection and is commonly found in the tuberculous. Soothing antiseptic applications serve best as local treatment.

2. Eczema of the lips as occurring in those with exudative diathesis. In these the lower lip is unduly prominent and frequently desquamative or herpetic with a tendency to fissure formation. These cases require constitutional treatment. The local applications are dependent on the existing condition; if the cracking is deep 60 per cent. lead plaster and 2 per cent. salicylic acid are used, or if there is much infiltration and they are of long standing radium is preferable.

3. The scurfy, scaly lip of the outdoor worker. In these the lips are dry, commonly scaly and tend to crack. This condition is most satisfactorily treated with radium.

4. Patches of hyperkeratosis. These resemble keratotic conditions on other parts and are commonly associated with them. They are also best treated with radium.

TOMLINSON, Omaha.

HYPOPHYSIS AND SCLERODERMA. GUIDO IZAR, Riforma med. **36**:482 (May 22) 1920.

The author makes a general survey of the literature of scleroderma and points to its relation to disturbances of the internal secretions, chiefly of the hypophysis. He relates the case of a girl, 7 years old, who presented a localized scleroderma of the right hand rapidly spreading to the rest of the body, being more marked on the neck and thorax. Provocative injections of epinephrin, atropin, thymus, ovarian and thyroid substances, produced no reaction. On the contrary, the injection of 0.25 and 0.5 c.c. of pituitary extract and hypophysin, produced a rise in temperature, increased blood pressure (from 70 to 108) and caused the pulse rate to become slow. Roentgen-ray examination of the skull showed an enlarged sella turcica, measuring 19 mm. by 7 mm.

The patient was treated with injections of pituitary extract and hypophysin on alternate days. After the sixth injection the condition began to improve and eight months later the patient had recovered. Only a few small areas of atrophic skin remained on the nape of the neck and on the wrist.

V. PARDO-CASTELLO, Havana.

COMMENT LES INDIGENES MAROCAINS SUIVENT LE TRAITEMENT DU LECHBA (HOW THE NATIVE MOROCCOANS FOLLOW THE TREATMENT OF LECHBA). POUPONNEAU, Paris méd. **10**:145 (March) 1920.

Under the heading of medical curiosities, Pouponneau describes the devotion of the native Moroccoans to the so-called lechba treatment for syphilis, which they continue to use in spite of the fact that intelligent treatment is offered them free. The generic term "lechba" includes a number of old methods of treatment based on a vegetable régime. Not only syphilis and everything connected with it is thus treated, but many unrelated conditions as well.

The Lechba el Aoud, employed in the treatment of the graver accidents of secondary syphilis, employs sarsaparilla root, while the Lechba el Iazir, less active, and used for syphilitic headache, arthritis, etc., employs *romarin* leaves.

Pouponneau describes in detail the method of carrying out these treatments.

SENEAR, Chicago.

UEBER DIE GOLDSOLREAKTION IM LIQUOR SYPHILITISCHER, DAS VERHALTEN ZU ANDEREN LIQUORREAKTIONEN AND IHRE KLINISCHE BRAUCHBARKEIT UND BEDEUTUNG (THE COLLOIDAL GOLD REACTION OF THE CEREBROSPINAL FLUID IN SYPHILITICS, ITS RELATION TO OTHER CEREBROSPINAL FLUID REACTION AND ITS CLINICAL VALUE AND APPLICABILITY). J. KYRLE, R. BRAUNT and F. MRAS, Wien. klin. Wchnschr. **33**:1, 1920.

The cerebrospinal fluid of the early syphilitic patient may show changes in constitution before any clinical signs are evident. These changes are not gross, but are of a complicated physicochemical nature.

The authors have examined 720 fluids. Unfortunately, they do not give the colloidal gold curve in full for their cases, merely indicating the reaction as —, ±, +, ++, +++. The cases were divided into nine groups from the seronegative primary syphilitic cases progressively to cases with tertiary clinical manifestations. The colloidal gold reaction was found to parallel, for the most part, the Wassermann reaction and the globulin findings. In many instances it was found to precede other positive tests and to indicate grave changes in the cerebrospinal fluid.

Reversals to negative findings are difficult to secure, despite vigorous therapeutic measures.

GOODMAN, New York.

STUDIES ON PIGMENT WITH THE DOPA-REACTION, ESPECIALLY IN CASES OF VITILIGO. ARNE KISSMEYER, Brit. J. Dermat. & Syph. **32**:156 (May) 1920.

Kissmeyer reviews Block's work with the "dopa-reaction," and then relates the result of its use in cases of vitiligo. He found that the pigmented portion of the skin gave a pronounced dopa-reaction, and was thus sharply demarcated from the nonreacting achromic portion of the skin. Microphotographs showing this, together with the apparent function of the dendritic pigment cells (melanoblasts of Block) are shown. Considering Bloch's theory of pigment production and his investigations, Kissmeyer concludes that the pathologic process in vitiligo is as follows:

"The vitiligo is an exhaustion dermatosis (Aufbrauchsdermatose), where the dopa-oxydase is used up on account of some unknown stimulant. In the extension of the process some cells or cell groups, which still react, are left in the achromic skin. By the very strong stimulation of the carbon arc-light baths the cells are induced to a more active dopa-oxydase production and the melanoblasts especially become very active; from the spots already pigmented they move into the achromic skin. It is not quite clear what their later destiny is. If they disappear after giving up their pigment (and oxydase?) to the cubical cells or if they themselves are changed into fixed epidermal cells is a question not yet clearly answered. That their rôle in pigment formation is a very important one is unquestionable.

SENEAR, Chicago.

THE FALLACY OF DEEP "IONIC MEDICATION." W. J. TURRELL, Am. J. Electrotherap. & Radiol. **38**:229 (July) 1920.

Ionic medication is defined as the attempt to obtain the specific action of certain drugs introduced into the tissues by means of the electric current. The writer states that the most direct proof against deep ionic medication is to be found in the failure to detect the presence of the drug deeper than the superficial layers of the skin after careful and thorough experimentation. He also maintains that the results obtained in ionic medication are not specific drug reactions, but are due to the electrolytic action of the galvanic current and that they are similar whether expensive drugs or common salt are employed for the solutions. Turrell states that this theory was sponsored in the eighteenth century and that its revival in the present day has led to much quackery prejudicial to the status of electrotherapy.

H. R. FOERSTER, Milwaukee.

THE ALKALI RESERVE IN PELLAGRA. M. X. SULLIVAN and R. E. STANTON, Arch. Int. Med. **26**:41 (July) 1920.

Examinations were made of fifty-six patients with pellagra in various stages using no medication and varying the diet only. They were tested for alkali reserve by the alveolar air method and by the determination of the carbon dioxid bound by the blood plasma. None showed marked depletion of the alkali reserve, about one-third were slightly below normal; the majority were within normal limits. The authors conclude from this work that there would seem to be little uncompensated acidosis in pellagra.

JAMIESON, Detroit.

STUDIES ON THE EFFECT OF LIGHT ON VITILIGO. CARL WITH, Brit. J. Dermat. & Syph. **32**:145 (May) 1920.

With's attention was called to the relation of vitiligo to light while working with light baths in the Finsen Institute. As a result of studies carried out he concludes:

1. During carbon arc-light baths vitiligo becomes visible in regions where formerly it was difficult to perceive; we have, on the other hand, not succeeded in producing new spots of vitiligo.
2. The carbon arc light produces on the patches of vitiligo a more or less decided macular pigmentation; this spreads from the periphery to the center, and may last fourteen months.
3. In three cases this pigmentary process continued after the light bath had ceased.
4. The vitiligo patches react with a stronger erythema than the pigmented skin, but little by little the patients are able to stand a quantity of light to which they formerly reacted with an erythema, not only on the pigmented but also on the vitiliginous regions of the skin. Consequently the organism is capable of protecting itself against the light in another way than by pigmentation.
5. The final proof has not yet been forthcoming that the rôle of the pigmentation is to form a protection against light. So many observations, however, tend to show that it must be considered as the most probable deduction.

SENEAR, Chicago.

PHYSIOTHERAPY IN THE TREATMENT OF CHRONIC SKIN DISEASES. J. M. E. PREVOST, Am. J. Electrotherap. & Radiol. **38**:235 (July) 1920.

As physiotherapeutic agents the writer names vibrotherapy, the static breeze, high frequency sparks and effluves, bi-electrolysis, hydro-electric baths, luminous baths, actinotherapy and the roentgen rays. The writer states that because of its efficiency against the cellular perversions of metabolism, physiotherapy ranks first in the rational curve of skin conditions. The roentgen rays are lauded in the treatment of hypertrichosis, nevus pigmentosus, trichophytosis and alopecia, but are otherwise given scant mention.

The other agents are enthusiastically referred to in the treatment of such conditions as nevi, acne, psoriasis, eczema, pruritis, sycosis, cancroids of the face and erythemas.

H. R. FOERSTER, Milwaukee.

NEOSALVARSANFALSCHUNGEN (SPURIOUS NEOSALVARSAN). L. Arzt, Wien. klin. Wchnschr. **33**:451, 1920.

There seems to be an organized trade in brands of spurious neosalvarsan, and the ampules, labels and containers, even to the seal have been cleverly counterfeited. In several instances, a number of original neosalvarsan tubes had been mixed with the others. [No doubt some of these products have reached this country. Physicians should take warning and not purchase so-called neosalvarsan of German make that is supposed to have been brought over by sea captains and the like. Recently I saw a doctor, who had purchased some of the "real" neosalvarsan, try to dissolve the stuff. A thick custard-like emulsion was the result. At the time of purchase, the seller had made a solution from another ampoule.]

Goodman, New York.

UEBER DIE NEUEN AUSFLOCKUNGSREAKTIONEN ZUR LUESDIAGNOSTIK IN BLUT UND LIQUOR (RECENT PRECIPITATION TESTS ON BLOOD AND CEREBROSPINAL FLUID IN SYPHILIS). Kafka, Dermat. wchnschr. **70**:385 (June 19) 1920.

Kafka discusses the technic of the Sachs-Georgi and the Meinecke tests. He describes with illustrations a new agglutinoscope for more exact reading of results. Both tests corresponded with the Wassermann in approximately 95 per cent. of the examinations. The Sachs-Georgi test seemed to be more sensitive in cases of primary syphilis and in treated cases. Kafka emphasizes the fact that these tests do not replace the Wassermann, but must be used in conjunction with it.

Zimmerman, Baltimore.

ROENTGENOGRAPHIC APPEARANCE, DIAGNOSIS AND PATHOLOGY OF SOME OBSCURE CASES OF BONE LESIONS. Robert W. Lovett and S. B. Wolbach, Surg., Gynec. & Obst. **31**:111 (Aug.) 1920.

Syphilis affects bones in two ways and results either in the destruction or the new formation of bone. Both are effects of the proliferative reaction to the causal agent, and both may occur in the same case. Destruction of bone follows the local, rapid formation of gummatous lesions, sometimes of endosteal and periosteal origin, sometimes perivascular and extending into bone. On the other hand, the degree of reaction of the spirochetes may be slight and result only in proliferation of cells of the periosteum and endosteum, the newly formed tissue developing osteoblasts and eventually, resulting in new deposits of bone. In one case, therefore, there is choking of normal bone by the gummatous process with its necrosis; in the other, merely stimulation of bone-forming tissue.

Goodman, New York.

ZUR ABORTIVBEHANDLUNG DER SYPHILIS (THE ABORTIVE TREATMENT OF SYPHILIS). Leven, Dermat. wchnschr. **70**:369 (June 12) 1920.

Leven protests against the dogmatic statement that cases of seronegative primary syphilis can be aborted by a single course of treatment. He cites the case of a patient treated with seven injections of the neosalvarsan brand of arsphenamin and thirty-two inunctions who developed a neurorecurrence

shortly after cessation of treatment. A second patient developed a reinduration three and one-half weeks after a course of ten 0.3 gm. doses of natrium-salvarsan.

ZIMMERMAN, Baltimore.

DIMAZON TO PROMOTE THE GROWTH OF HAIR. I. SAUDEK, Dermat. Centralbl. (May) 1920.

For eight years Dr. Saudek has been using dimazon in the treatment of alopecia areata. He has treated forty cases of the disease with this drug. In two to three weeks, he claims, the hair begins to return. Even in cases of alopecia following seborrhea the hair is regenerated to a certain extent. In ten cases of alopecia following influenza he thought that this drug hastened the return of the hair. He uses it in a 2 per cent. ointment and directs that it be thoroughly massaged into the bald areas, twice daily. He did not use the ultraviolet rays in any of these cases, but suggests that the combined use of these remedies may give even better results

HEITHAUS, Cleveland.

KERATODERMA BLENNORRHAGICA: IS IT A FORM OF PSORIASIS? H. G. ADAMSON, Brit. J. Dermat. & Syph. **32**:183 (June) 1920.

Adamson saw several cases in which patients suffering with rheumatoid arthritis associated with more or less extensive psoriasis of the limbs and trunk, had heaped-up horny looking lesions of the palms and soles, bearing a close resemblance to the horny-looking cones of gonorrheal hyperkeratosis. Coupling this observation with the fact that in many cases of keratoderma blennorrhagica psoriasis or a psoriasiform eruption on the other parts of the body had been noted, and recalling the similar microscopic pictures in the two conditions, he speculates on the possibility that psoriasis may be due to some micro-organism bearing a family relationship with the gonococcus.

SENEAR, Chicago.

THE INFLUENCE OF ROENTGEN RAYS IN THE DISEASES OF THE SKIN. JAY FRANK SCHAMBERG, Am. J. Electrotherap. & Radiol. **38**:239 (July) 1920.

This article is a concise, authoritative review on this subject. A note of warning is sounded regarding persistent treatment with the roentgen ray of any condition which fails to respond. The author points out that vascular changes with resulting devitalization of tissues is likely to result, rendering other methods of treatment ineffective. Filtered rays are advocated in the treatment of herpes zoster in preference to galvanism.

H. R. FOERSTER, Milwaukee.

LE NEURALGIE SCIATIQUE D'ORIGINE SYPHILITIQUE (SCIATICA OF SYPHILITIC ORIGIN). G. BOUDET, Gaz. d. hop. **93**:727, 1920.

In 150 soldiers with sciatica, excluding all cases that might be ascribed to trauma or to a neurosis, the Wassermann test was found to be positive in 38.66 per cent. Clinically the sciatica due to syphilis does not differ from that of other origin; however, the following points suggest syphilis; nocturnal exacerbation, pain in the distribution of other nerves than the sciatic and chronicity. No data as to spinal fluid examination are given.

ZIMMERMAN, Baltimore.

LATE HEREDITARY SYPHILIS. MEMBRANOUS PERICOLITIS, PERIENTERITIS, OR CHRONIC ABDOMINAL SYNDROME. M. R. Castex and Delfor Del Valle, Surg., Gynec. & Obst. **31**:160 (Aug.) 1920.

As the result of medical and surgical studies in Argentina, the authors conclude that hereditary syphilis is a very frequent—perhaps the most frequent—cause of membranous perienteritis and analogous conditions, as described by Lane, Jackson, Wilms and others. It is to be noted that although the efficacy of mercurial treatment had been noted, syphilis, either acquired or hereditary, had never previously been mentioned as a possible cause of this condition.

Goodman, New York.

A SYPHILIZED FAMILY. G. R. Hamilton, Brit. J. Dermat. & Syph. **32**:163 (May) 1920.

Hamilton saw a boy aged 10 years, who had a mixed eruption of psoriasis and syphilis. The Wassermann reaction was positive. Investigation showed the father and the two youngest children had negative Wassermann reactions, while the mother and three older children all had positive reactions. The question as to whether the condition in the children was acquired or congenital arises. The three infected children had all had "tonsillitis" about six weeks before the boy was first seen, but otherwise there were no signs or history of syphilis in any one except the first patient. It is the author's opinion that the condition in the children was acquired.

Senear, Chicago.

A CASE OF OCULAR PEMPHIGUGS. William Campbell Posey, Am. J. Ophth. **3**:507 (July) 1920.

Posey reports a case in a young adult colored woman, associated with a chronic recurrent dermatitis, which had been diagnosed as Duhring's disease by two dermatologists. Clinical records are presented for both the eye and skin condition, and it is noted that the latter was associated with mucous membrane lesions of the mouth and lips. The author does not dispute the dermatologic diagnosis, considering the differentiation of pemphigus and dermatitis herpetiformis as chiefly an academic question.

H. R. Foerster, Milwaukee.

UEBER EINEN UEBERGANGSFALL ZUR SCABIES NORWEGICA (A TRANSITIONAL CASE OF SCABIES NORWEGICA). L. Kumer, Wien. klin. Wchnschr. **33**:271, 1920.

Although Boeck described so-called scabies norwegica in 1848, only fifty cases have been found in the literature. Kumer had the opportunity of studying a case of progressive muscular dystrophy in which scabies was present. The lesions in the palm approximated those seen in Norwegian scabies, especially in the number of burrows present, and the comparative ease of demonstrating the ova. In the histologic sections, from four to six burrows were demonstrable in each centimeter of tissue. The patient also presented the picture of ordinary scabies.

Goodman, New York.

DIE MALIGNE ENTARTUNG VON SALVARSAN-HG-EXANTHEMEN —EXFOLIIERENDE GENERALISIERTE ERYTHRODEMIE (A MALIGNANT FORM OF SALVARSAN-MERCURY DERMATOSES—GENERAL EXFOLIATIVE DERMATITIS). HERMANN, Dermat. wchnschr. **70**:401 (June 26) 1920.

Hermann reports the case of a dermatitis, developing after combined treatment with the neosalvarsan brand of arsphenamin and mercury, which assumed all the characteristics of an "erythrodermie exfoliante generalisée secondaire" of Brocq.

ZIMMERMANN, Baltimore.

LES "PILULES DE DUPUYTREN" (DUPUYTREN'S PILLS). R. A. GUTMAN, Paris méd. **10**:138 (March) 1920.

Gutman gives the various formulas and modifications for Dupuytren's pills, and publishes an autographed prescription of Dupuytren's which was apparently written before 1832 and probably represents the original and unedited formula for these pills, as follows: Extract of guaiac, 4 grains; extract of fumaria, 4 grains; aqueous extract of opium, ½ grain, and mercuric chlorid, ¼ grain.

SENEAR, Chicago.

ZUR SERODIAGNOSE DER LUES MITTELST NEUERER PRAEZIPITATIONSREAKTIONEN (SERODIAGNOSIS OF SYPHILIS BY NEW PRECIPITATION REACTIONS). L. KIRSCHNER and J. SEGALL, Wien. klin. Wchnschr. **33**:377, 1920.

The authors have used the precipitation test of Sachs and Georgi in conjunction with the Wassermann test in about 1,000 cases. They believe that it has a certain value in latent syphilis.

GOODMAN, New York.

MERCURY BICHLORID INTRAVENOUSLY. C. H. BASTRON, Am. J. Med. Sc. **160**:118 (July) 1920.

In cases in which quick results must be obtained the author advocates using mercuric chlorid in normal salt solution, giving 0.1 of a grain two or three times weekly, increasing the dose slowly up to a point short of salivation. The greatest danger to be avoided is thrombosis. This can be lessened by suspension of the mercury in serum before injection.

JAMIESON, Detroit.

A CASE OF KERATODERMA BLENNORRHAGICA IN A WOMAN. C. LEONARD ISAAC, Brit. J. Dermat. & Syph. **32**:195 (June) 1920.

This clinical note records a case of keratoderma blennorrhagica which is unusual in that the patient was a woman. Graham Little, in 1918, drew attention to the fact that no authentic case had been observed in a woman.

SENEAR, Chicago.

UEBER EINIGE HAUTVERAENDERUNGEN BEI TIEREN (SOME SKIN CHANGES IN ANIMALS). B. Lipschutz, Wien. klin. Wchnschr. **33**:426, 1920.

A presentation of animals with affections of the skin. Scabies of rats, and molluscum contagiosum of pigeons were among those demonstrated.

Goodman, New York.

THE EFFECTS OF TUBERCULIN IN LUPUS VULGARIS. Robert Aitken, Edinburgh M. J. **24**:4 (April) 1920.

In view of the fact that statements have been made that in the treatment of lupus vulgaris tuberculin not only does no good, but interferes with the efficacy of other remedies, the writer, at the request of Dr. Norman Walker, investigated the cases which had been so treated.

The cases reviewed fall into two main classes, namely, those treated exclusively with Koch's New Tuberculin (T. R.) and those in which Koch's Original Tuberculin (O. T.) was given. All patients improved, even those who received a short course of tuberculin. The drug is not held out as the only way of curing lupus, nor as the best way of treating all patients, but there does not seem to be any evidence in the series of cases under review that the injections prevented any other remedy doing good.

Levin, New York.

ROENTGEN-RAY TREATMENT OF VERRUCAE PLANTARIS. H. H. Hazen and F. J. Eichenlaub, J. A. M. A. **74**:1311 (May 8) 1920.

The authors report the records of sixteen cases of plantar warts treated by the roentgen ray. Some of those of longest duration responded most quickly to treatment, and neither size nor location appeared to play any part. Almost invariably the pain disappeared in from two to four days after the first treatment. Their technic is to give 1½ Holzknecht skin units every three or four weeks, the dosage being estimated according to the method long advocated by MacKee. When the lesion has disappeared, they usually give an additional treatment to be sure of a complete cure. They use no filter in this work, as they feel that on superficial lesions results are much better with the unfiltered ray. The cure seems to be permanent.

Waugh, Chicago.

UEBER DEN KLINISCHEN WERT DER AUSFLOCKUNGSREACTION NACH SACHS UND GEORGI (CLINICAL VALUE OF SACHS-GEORGI PRECIPITATION REACTION). Ludwig Kleeberg, Dermat. Wchnschr. **70**:33 (Jan.) 1920.

The Sachs-Georgi and Wassermann tests corresponded in 89.6 per cent. of 1,112 serums examined. In forty-three cases, in which the Wassermann test was positive and the diagnosis of syphilis was unquestionable the Sachs-Georgi reaction was negative. Sixteen of the patients presented secondary lesions; in the thirteen which returned for reexamination the Sachs-Georgi reaction subsequently became positive. In six cases of secondary syphilis the Wassermann test was negative, the Sachs-Georgi positive. In six cases of tertiary syphilis and parasyphilis the Wassermann test was positive, the

Sachs-Georgi negative; in ten similar cases the Sachs-Georgi was positive, the Wassermann negative. Under treatment the Sachs-Georgi reaction became negative more slowly than the Wassermann.

ZIMMERMANN, Baltimore.

UEBER DIE BEHANDLUNG VON TAETOWIERUNGEN (REMOVAL OF TATTOO MARKS). STUTZMANN, Dermat. Wchnschr. **70:** No. 5 (Jan.) 1920.

After a review of the various methods for removing tattoo marks the author gives his experience in treating a case in which the skin was filled with carbon particles following the explosion of a bomb. The best result was obtained by application of moist pepsin dressings after the affected parts had been subjected to multiple punctures with tattoo needles. This treatment was kept up for seven months after which the dark particles in the skin had assumed a grayish color and in some places seemed to have entirely disappeared.

The author also obtained good results in a tattoo mark by retattooing the area with a 45 per cent. solution of zinc chlorid.

KETRON, Baltimore.

ULCUS TROPICUM TREATED WITH TARTAR EMETIC. A. MEI, J. Trop. M. **23**:38 (Feb. 2) 1920.

In addition to intravenous use, this drug can be applied locally with great efficiency, according to the author. It should be applied carefully to the edges of the ulcer, only a small amount of powder being used. The local reaction may be rather severe, but the organisms begin to disappear in two or three days and are practically gone in two weeks. The spirochetes first disappear, Vincent's bacilli and cocci remaining much longer even though the ulcer improves before they have disappeared. For this reason the author thinks that the *Spirochaeta Schaudinni* is the true etiologic factor and that Vincent's bacilli are symbiotic and have no pathologic significance.

JAMIESON, Detroit.

VENEREAL PROPHYLAXIS. P. M. ASHBURN, J. A. M. A. **74**:1314 (May 8) 1920.

In order to determine, if possible, whether the use of prophylaxis prevents one type of venereal disease more than another, a comparison was made by Ashburn of the relative proportions of the three diseases in the first 2,000 cases in which infection followed the use, and in the first 2,000 cases in which it followed neglect of prophylaxis. The results were: without prophylaxis, gonorrhea, 67.2 per cent.; chancroid, 15.6 per cent.; syphilis, 17.2 per cent.; with prophylaxis, gonorrhea, 64.5 per cent.; chancroid, 18.9 per cent., and syphilis, 16.6 per cent.

WAUGH, Chicago.

ANTHRAX FROM THE SHAVING-BRUSH AND PRIMARY ANTHRAX MENINGITIS. H. W. CAREY, Am. J. Med. Sc. **159**:742 (May) 1920.

Attention is directed to the number of cases of anthrax since 1914, especially in England and in concentration camps. In the case reported the patient was infected without question by a new, cheap shaving brush used for the first time the day before the pustular lesion began. Complete recovery followed excision. Most of the infections were found to be due to the use of

horsehair and pig bristles imported from China and Siberia and used in manufacturing shaving brushes. Direct cultural attempts were unsuccessful, due to the large overgrowth of adventitious organisms.

Nine instances of meningeal infection have been reported, of which three were apparently primary. Septicemia and intestinal or pneumonic infection have also occurred.

JAMIESON, Detroit.

CAS DE LUPUS ERYTHEMATEUX PLANTAIRE (CASE OF PLANTAR ERYTHEMATOUS LUPUS). PARIN and PÉRIN, Bull. Soc. franç. dermat. et syph. No. 8, 1919.

Parin and Périn describe a case of lupus erythematosus in which typical lesions of the face and hands are associated with lesions on the soles. The lesions in the latter site are described in detail, and have some points in common with lupus erythematosus of the face, although the general aspect is different. The diagnosis was also supported by microscopic examination of the excised tissue.

SENEAR, Chicago.

UEBER DIE UEBERTRAGBARKEIT DES HERPES SIMPLEX AUF DIE KANINCHENHORNHAUT (THE TRANSMISSION OF HERPES SIMPLEX TO CORNEA OF RABBITS). OSKAR BAUM, Dermat. Wchnschr. **70**:105 (Feb.) 1920.

This work is a repetition of that of Löwenstein who was able to transmit herpes simplex in fourteen instances to the corneas of rabbits (*München. med. Wchnschr.*, 1919, No. 28). Baum was successful in seven cases and in one instance transmitted the disease from the cornea of one rabbit to that of another. He was unable, however, to transmit in a like manner other vesicular conditions, such as herpes zoster, eczema, pemphigus, etc. The author believes that the inability to transmit herpes zoster speaks for the sharp differentiation of this disease from herpes simplex.

KETRON, Baltimore.

UNSERE ERFAHRUNGEN MIT SULFOXYLAT (EXPERIENCES WITH SULPHOXYLAT). GUSTAV FANTL, Dermat. Wchnschr. **70**: 155 (March) 1920.

Sulphoxylat, a new arsphenamin derivative made by Kolle, was found to be inferior to arsphenamin in its sterilizing power. In some cases repeated doses were necessary to cause the disappearance of spirochetes from lesions.

ZIMMERMANN, Baltimore.

MEINE BEHANDLUNG DER TRICHOPHYTIA UND SYCOSIS BARBAE (MY TREATMENT OF TRICHOPHYTOSIS AND SYCOSIS BARBAE). J. WETTERER, Dermat. Wchnschr. **70**:87 (Feb.) 1920.

The treatment consists of various combinations of antiseptics, ultraviolet light, roentgen ray and electrolysis, depending on the type of disease treated. The author claims cure in 98 per cent. of cases. For detail of treatment the reader should consult original article.

KETRON, Baltimore.

CASE OF APPARENT DIPHTHEROID INFECTION OF THE SKIN. H. W. BARBER, Proc. Roy. Soc. Med. **13**:40 (March) 1920.

Beginning as a boil on the dorsum of the left wrist, the patient developed spreading lesions on the left forearm, right calf and left leg. The Wassermann reaction and repeated examinations for the streptothrix and sporothrix were negative. Finally a diphtheroid organism was isolated from the deep skin layers which proved pathogenic to animals and was agglutinated by the patient's serum. After repeated failures by different lines of therapy, an autogenous vaccine was given and the patient made a rapid recovery.

GUY, Pittsburgh.

THE CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS. J. E. MOORE, Arch. Int. Med. **25**:58 (Jan.) 1920.

On account of the frequency of finding a "paretic" colloidal gold curve in cases of multiple sclerosis, the writer has analyzed the spinal fluid findings in twenty-eight cases showing that the curve mentioned is not typically syphilitic with other findings negative. Sixteen of these cases showed a pleocytosis (above 5); globulin was positive in twenty-five, while blood and spinal fluid Wassermann reactions were negative. Eighteen cases showed a paretic gold curve, seven were negative and three syphilitic.

He thinks the picture presented in these spinal fluid findings is strong evidence of multiple sclerosis.

JAMIESON, Detroit.

THE ROENTGEN-RAY TREATMENT OF VERRUCA PLANTARIS. H. H. HAZEN, J. A. M. A. **74**:19 (May 8) 1920.

Sixteen cases of verruca plantaris were treated by the roentgen ray with success and apparent permanent cure. The technic consisted in giving 11/3 Holzknecht skin units every three to four weeks. From two to seven treatments were given to obtain a cure.

LEVIN, New York.

CASE OF ERYTHEMA INDURATUM IN YOUNG GIRLS, ASSOCIATED WITH FOLLICLIS AND PHLYCTENULAR ULCERS. GEORGE PERNET, Proc. Roy. Soc. Med. **13**:53 (March) 1920.

This article discusses a case of Bazin's disease affecting the right calf and associated with folliclis lesions on the back of the hands, phlyctenular ulcers and chilblains. There were two patients with active tuberculosis in the family. It was proposed to give the patient chaulmoogra oil treatment.

GUY, Pittsburgh.

SADD DERMATITIS. A. J. CHALMERS and A. F. JOSEPH, J. Trop. M. **23**:57 (March 1) 1920

This dermatitis is an irritating, small papular eruption caused by coming in contact with small hairs which grow on certain grass in the upper Nile

region. The action is purely local and probably entirely mechanical, although the hairs are hollow and may contain a toxin. Thorough removal with soap and water followed by a bland lotion will quickly cure the condition.

JAMIESON, Detroit.

UEBER BEOBACHTUNG VON SPIROCHAETEN IM HAENGENDEN TROPFEN BEI DUNKELFELDBELEUCHTUNG (OBSERVATION OF SPIROCHETES IN HANGING DROP PREPARATIONS WITH DARK FIELD ILLUMINATION). F. W. OELZE, Dermat. Wchnschr. **70**:1 (Jan.) 1920.

According to Oelze, this method is especially suitable for the study of motility of spirochetes. A detailed description of the apparatus is given.

ZIMMERMANN, Baltimore.

UEBER EINE HAUSEPIDEMIE VON HAARAUSFALL BEI SAUGLINGEN (A HOSPITAL EPIDEMIC OF LOSS OF HAIR IN INFANTS). OSKAR HELLER, Dermat. Wchnschr. **70**:145 (March) 1920.

Ten infants from 4 weeks to 6 months of age were affected with a sudden loss of hair during a period of about three weeks. The loss of hair was complete with mild inflammatory reaction, but returned after a short period. No etiologic factor could be determined.

KETRON, Baltimore.

ZUR THERAPIE DER PARAPSORIASIS MIT PILOKARPIN (THE TREATMENT OF PARAPSORIASIS WITH PILOCARPIN). LÖWENSTEIN, Dermat. Wchnschr. **70**:4 (Jan.) 1920.

The author describes a case of "parapsoriasis en goutte" cured by the intramuscular injection of pilocarpin hydrochlorid. The first injection consisted of 0.005 gm., the succeeding ones, 0.01 gm. The first five injections were given every other day, the sixth after a five day interval and the last after an eight day interval. Excessive sweating, erythema and occasionally nausea and salivation were observed but there were no alarming symptoms. Eight days after the last injection the disease had entirely disappeared.

KETRON, Baltimore.

PHAGEDENA OF HUNTERIAN CHANCRE FOLLOWING TREATMENT WITH NOVARSENOBENZOL. H. M. HANSCHELL, Brit. M. J. **1**:498 (April 10) 1920.

The author reports two cases of Hunterian chancre, one intra-urethral, the other on the mid-dorsum of the glans penis, in which there was bacterial infection existing with the syphilitic infection. In both cases injections of novarsenobenzol were given, and in both cases gangrene and marked destruction of tissue occurred in the chancre.

He concludes that the effect of the reaction from novarsenobenzol was to damage still further the chancre tissue already damaged by the spirochetes.

OLIVER, Chicago.

CASE OF LEPROSY DEMONSTRATING THE VALUE OF A TISSUE VACCINE. A. WINKELRIED WILLIAMS, Proc. Roy. Soc. Med. **13**:50 (March) 1920.

This article concerns a proven case of lepra apparently cured by the use of a vaccine prepared from autogenous lepromas. Dr. Castellani, in discussing the cases, called attention to the fact that Dr. Nichols and he had employed the same technic in 1905 with rather disappointing results. He considered the present improvement evidence of the infection being dormant and spoke favorably of the efficacy of chaulmoogra oil as a palliative.

GUY, Pittsburgh.

SOME FURTHER OBSERVATIONS ON THE ETIOLOGY OF PELLAGRA. A. VISWALINGAM, J. Trop. M. **23**:46 (Feb. 16) 1920.

The notes given in this article tend to confirm the opinion stated before by the writer that pellagra is primarily a gastro-intestinal disorder induced by low protein diet, unhygienic surroundings, lack of sunlight, etc., followed by an infection which gains entrance through the gastro-intestinal tract.

JAMIESON, Detroit.

EIN BEITRAG ZUR SICHTBAREN LYMPHANGITIS TUBERCULOSA (VISIBLE TUBERCULOUS LYMPHANGITIS). WILHELM KIENDL, Dermat. Wchnschr. **70**: No. 4 (Jan.) 1920.

The author describes, for illustration, a case of tuberculous lymphangitis and gives the differential points between this disease and the lymphangitis of sporotrichosis, syphilis and cancer. He sums up the characteristics of the disease: 1. The presence of a tuberculous "primary lesion" usually lupus, tuberculous ulcer or a postmortem tubercle, or the lymphangitis may be associated with bone or joint tuberculosis. 2. There are palpable, thickened, nodular cords running centrally from the primary lesions. 3. Chronic swelling of the regional lymph gland is often present. 4. If the nodules soften and break through the skin, typical tuberculous ulcers with irregular, undermined edges are formed. 5. The course of the disease is slow and chronic, the fever is slight and there is little pain.

KETRON, Baltimore.

Book Review

OCCUPATIONAL AFFECTIONS OF THE SKIN: THEIR PREVENTION AND TREATMENT WITH AN ACCOUNT OF THE TRADE PROCESSES AND AGENTS WHICH GIVE RISE TO THEM. R. Prosser White, M.D., Ed.M.R.C.S. Second edition with 24 plates. London, H. K. Lewis & Co., 1920. Pp. 360.

White, in the second edition of his excellent publication, gives a volume of discussion of the salient features of the occupational affections of the skin as encountered in his own practice and as gleaned from the literature of other countries. The conditions caused by the industries peculiar to the recent war are included in this volume.

The book is, however, broader in scope than its name implies for the whole subject of dermatoses of external origin is considered. It is, therefore, of special value to the dermatologist who will find in this collected and systematized study a truly remarkable fund of significant information on the diagnosis and differential diagnosis of a highly specialized field. The second edition is far superior to the first; it contains many new features, and a broader consideration of the topics of the earlier edition.

White objects to the terms "eczema" and "dermatitis" as applied to the occupational affections of the skin, and thinks it is more convenient and logical to use the noncommittal word "dermatopathy" or "dermapathy" or the less correct but more usual "dermatosis"—disease of the skin. Any of these terms embrace trade lesions of an eczematous type, as well as dissimilar examples of skin disease caused by various occupations. When possible the name of the offending agent should be prefaced, and when this is uncertain, "traumatic," "occupational" or "professional" should be added.

The effects of lightning, roentgen ray, radium, heat and sun rays with their sequelae are carefully given. Dermatitis venenata is accorded a special chapter, and the modern experimental work on immunization and sensitization with the poison ivy, sumac and nettle is included in the discussion of the anaphylactic origin of this group. The ever increasing importance of such diseases as erysipeloid of Rosenbach, postmortem wart, anthrax, glanders, blastomycosis and the other dermatoses induced by insects and vegetables are mirrored by the liberal space allotted to them. A chapter on war dermatoses and their relation to postbellum civilian practice closes the volume.

There are numerous references, which are thoroughly up to date. About sixty pages of the book are occupied by the index. These features will prove a boon to the inquirer.

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